

DAFTAR PUSTAKA

Abbott, C.A., Malik, R.A., Ross, E.R.E. van, Kulkarni, J., dan Boulton, A.J.M., 2011. Prevalence and Characteristics of Painful Diabetic Neuropathy in a Large Community-Based Diabetic Population in the UK. *Diabetes Care*, **34**: 2220–2224.

Abdulrazaq, N.B., Cho, M.M., Win, N.N., Zaman, R., dan Rahman, M.T., 2012. Beneficial effects of ginger (*Zingiber officinale*) on carbohydrate metabolism in streptozotocin-induced diabetic rats. *British Journal of Nutrition*, **108**: 1194–1201.

Afifah, 2016. 'Pengaruh Pemberian Minyak Jahe Merah (*Zingiber officinale* var. *rubrum*) pada Mencit Neuropati dengan Metode Partial Sciatic Nerve Ligation (PSNL)', , *Skripsi, Sarjana Farmasi*, . Fakultas Farmasi, Universitas Negeri Jember, Jember.

Akbarzadeh, A., Norouziyan, D., Mehrabi, M.R., Jamshidi, S., Farhangi, A., Allah Verdi, A., dkk., 2007. Induction of diabetes by Streptozotocin in rats. *Indian Journal of Clinical Biochemistry*, **22**: 60–64.

Akhani, S.P., Vishwakarma, S.L., dan Goyal, R.K., 2004. Anti-diabetic activity of *Zingiber officinale* in streptozotocin-induced type I diabetic rats. *The Journal of pharmacy and pharmacology*, **56**: 101–5.

Al-Amin, Z.M., Thomson, M., Al-Qattan, K.K., Peltonen-Shalaby, R., dan Ali, M., 2006. Anti-diabetic and hypolipidaemic properties of ginger (*Zingiber officinale*) in streptozotocin-induced diabetic rats. *The British journal of nutrition*, **96**: 660–666.

Al-Nahain, A., Jahan, R., dan Rahmatullah, M., 2014. *Zingiber officinale* : A Potential Plant against Rheumatoid Arthritis. *Arthritis*, **2014**: 1–8.

Al-Qattan, K., Thomson, M., dan Ali, M., 2008. Garlic (*Allium sativum*) and

ginger (*Zingiber officinale*) attenuate structural nephropathy progression in streptozotocin-induced diabetic rats. *e-SPEN, the European e-Journal of Clinical Nutrition and Metabolism*, **3**: 62–71.

Ali, B.H., Blunden, G., Tanira, M.O., dan Nemmar, A., 2008. Some phytochemical, pharmacological and toxicological properties of ginger (*Zingiber officinale* Roscoe): A review of recent research. *Food and Chemical Toxicology*, **46**: 409–420.

Almasyhuri, Sri Wardatun, dan Leni Nuraeni, 2012. Perbedaan Cara Pengirisan dan Pengeringan terhadap Kandungan Minyak Atsiri dalam Jahe Merah. *Buletin Penelitian Kesehatan*, **40**: 123–129.

Aly, U.I., Abbas, M.S., Taha, H.S., dan Gaber, E.-S.I., 2013. Characterization of 6-Gingerol for In Vivo and In Vitro Ginger (*Zingiber officinale*) Using High Performance Liquid Chromatography. *Global Journal Of Botanical Science*, **1**: 9–17.

Andallu, B., Radhika, B., dan Suryakantham, V., 2004. Effect of aswagandha, ginger and mulberry on hyperglycemia and hyperlipidemia. *Plant Foods Hum Nutr*, **58**: 1–7.

Anjaneyulu, M. dan Chopra, K., 2003. Quercetin, a bioflavonoid, attenuates thermal hyperalgesia in a mouse model of diabetic neuropathic pain. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, **27**: 1001–1005.

Anonim, 2009. KMK Republik Indonesia Nomor 261/SK/MENKES/IV/2009 Tentang Farmakope Herbal Indonesia.

Arnold, J.T., Stewart, S.B., dan Sammut, L., 2017. Oral Capsaicin Ingestion : A Brief Update-Dose, Tolerance and Side Effects. *Research and Reviews: Journal of Herbal Sciences*, **5**: 1–5.

- Backonja, M. dan Glanzman, R.L., 2003. Gabapentin dosing for neuropathic pain: Evidence from randomized, placebo-controlled clinical trials. *Clinical Therapeutics*, **25**: 81–104.
- Bahadur Singh, A., Singh, N., Maurya, R., dan Kumar Srivastava, A., 2009. Anti-hyperglycaemic, lipid lowering and anti-oxidant properties of [6]-gingerol in db/db mice. *International Journal of Medicine and Medical Sciences*, **1**: 536–544.
- Bansal, S., Siddarth, M., Chawla, D., Banerjee, B.D., Madhu, S. V., dan Tripathi, A.K., 2012. Advanced glycation end products enhance reactive oxygen and nitrogen species generation in neutrophils in vitro. *Mol Cell Biochem*, **361**: 289–296.
- Basbaum, A.I., Bautista, D.M., Scherrer, G., dan Julius, D., 2009. Cellular and Molecular Mechanisms of Pain. *Cellular*, **139**: 267–284.
- Basith, S., Cui, M., Hong, S., dan Choi, S., 2016. Harnessing the therapeutic potential of capsaicin and its analogues in pain and other diseases. *Molecules*, **21**: 1–28.
- Benarroch, E.E., 2008. TRP Channels Functions and Involvement in Neurologic Disease. *Neurology*, **70**: 648–652.
- Benham, C.D., Gunthorpe, M.J., dan Davis, J.B., 2003. TRPV channels as temperature sensors. *Cell Calcium*, **33**: 479–487.
- Bhatt, L.K. dan Veeranjanyulu, A., 2010. Minocycline with aspirin: A therapeutic approach in the treatment of diabetic neuropathy. *Neurological Sciences*, **31**: 705–716.
- Bhattarai, S., Tran, V.A.N.H., dan Duke, C.C., 2001. The Stability of Gingerol and Shogaol in Aqueous Solutions. *Journal of Pharmaceutical Sciences*, **90**: 1658–1664.

- Bishnoi, M., Bosgraaf, C.A., Abooj, M., Zhong, L., dan Premkumar, L.S., 2011. Streptozotocin-Induced Early Thermal Hyperalgesia is independent of Glycemic State of Rats: Role of Transient Receptor Potential Vanilloid 1 (TRPV1) and Inflammatory mediators. *Molecular Pain*, **7**: 1–11.
- Bode, A.M. dan Dong, Z., 2011. The Amazing and Mighty Ginger, dalam: IFF, B. dan S, W.-G. (Editor), *Herbal Medicine: Biomolecular and Clinical Aspects*. CRC Press/Taylor & Francis, Boca Raton (FL).
- Bohlen, H.G., 2004. Protein kinase betaII in Zucker obese rats compromises oxygen and flow-mediated regulation of nitric oxide formation. *American journal of physiology. Heart and circulatory physiology*, **286**: 492–497.
- Brederson, J.-D., Kym, P.R., dan Szallasi, A., 2013. Targeting TRP channels for pain relief. *European Journal of Pharmacology*, **716**: 61–76.
- Brownlee, M., 2001. Biochemistry and molecular cell biology of diabetic complications. *Nature*, **414**: 813–820.
- Bujak, J.K., Kosmala, D., Szopa, I.M., Majchrzak, K., dan Bednarczyk, P., 2019. Inflammation, Cancer and Immunity—Implication of TRPV1 Channel. *Frontiers in Oncology*, **9**: 1–16.
- Callaghan, B.C., Cheng, H.T., Stables, C.L., Smith, A.L., dan Feldman, E.L., 2012. Diabetic neuropathy: clinical manifestations and current treatments. *The Lancet Neurology*, **11**: 521–534.
- Castagné, V., Hernier, A.M., dan Porsolt, R.D., 2014. CNS Safety Pharmacology. *Reference Module in Biomedical Sciences*, 1–12.
- Caterina, M., Leffler, A., Malmberg, A., Martin, W., Trafton, J., Petersen-Zeitz, K., dkk., 2000. Impaired nociception and pain sensation in mice lacking the capsaicin receptor. *Science*, **288**: 306–313.
- Cazes, J. (Editor), 2010. *Encyclopedia of Chromatography*, 3rd ed. CRS Press

Taylor & Francis Group, Boca Raton, London, New York.

Chakraborty, D., Mukherjee, A., Sikdar, S., Paul, A., Ghosh, S., dan Khuda-Bukhsh, A.R., 2012. [6]-Gingerol isolated from ginger attenuates sodium arsenite induced oxidative stress and plays a corrective role in improving insulin signaling in mice. *Toxicology Letters*, **210**: 34–43.

Charan, J. dan Kantharia, N., 2013. How to calculate sample size in animal studies? *Journal of Pharmacology and Pharmacotherapeutics*, **4**: 303–307.

Chaudhry¹, Z.Z., 2013. Streptozotocin is equally diabetogenic whether administered to fed or fasted mice. *Laboratory Animals*, **47**: 257–265.

Chrubasik, S., Pittler, M.H., dan Roufogalis, B.D., 2005. *Zingiberis rhizoma*: A comprehensive review on the ginger effect and efficacy profiles. *Phytomedicine*, **12**: 684–701.

Chundi, V., Challa, S.R., Garikapati, D.R., Juvva, G., Jampani, A., Pinnamaneni, S.H., dkk., 2016. Biochanin-A attenuates neuropathic pain in diabetic rats. *Journal of Ayurveda and Integrative Medicine*, **7**: 231–237.

de Campos Lima, T., Santos, D. de O., Lemes, J.B.P., Chiovato, L.M., dan Lotufo, C.M. da C., 2019. Hyperglycemia induces mechanical hyperalgesia and depolarization of the resting membrane potential of primary nociceptive neurons: Role of ATP-sensitive potassium channels. *Journal of the Neurological Sciences*, **401**: 55–61.

Deeds, M., Anderson, J., Armstrong, A., Gastineau, D., Hiddinga, H., Jahangir, A., dkk., 2011. Single Dose Streptozotocin Induced Diabetes: Considerations for Study Design in Islet Transplantation Models. *Laboratory Animals*, **45**: 131–140.

- Dewanjee, S., Das, S., Kumar, A., Bhattacharjee, N., dan Dihingia, A., 2018. Molecular mechanism of diabetic neuropathy and its pharmacotherapeutic targets. *European Journal of Pharmacology*, **833**: 472–523.
- Dillingham, T.R., Pezzin, L.E., dan Shore, A.D., 2005. Reamputation, mortality, and health care costs among persons with dysvascular lower-limb amputations. *Archives of Physical Medicine and Rehabilitation*, **86**: 480–486.
- Du, Q., Liao, Q., Chen, C., Yang, X., Xie, R., dan Xu, J., 2019. The Role of Transient Receptor Potential Vanilloid 1 in Common Diseases of the Digestive Tract and the Cardiovascular and Respiratory System. *Frontiers in Physiology*, **10**: 1–17.
- Dubin, A.E. dan Patapoutian, A., 2010. Nociceptors : the sensors of the pain pathway Find. *Journal of Clinical Investigation*, **120**: 3760–3772.
- Duran-jimenez, B., Dobler, D., Moffatt, S., Rabbani, N., Streuli, C.H., Thornalley, P.J., dkk., 2009. Advanced Glycation End Products in Extracellular Matrix Proteins Contribute to the Failure of Sensory Nerve Regeneration in Diabetes. *Sensory Neuron*, **58**: 2893–2903.
- Dyck, P.J. dan Giannini, C., 1996. Pathologic Alteration in the Diabetic Neuropathies of humans : A Review. *Journal of Neuropathology and Experimental Neurology*, **55**: 1181–1193.
- E, J., R, V., dan T, J.Z., 2014. Quality of dry ginger (*Zingiber officinale*) by different drying methods. *Journal of Food Science and Technology*, **51**: 3190–3198.
- Ebata-Kogure, N., Nozawa, K., Murakami, A., Toyoda, T., Haga, Y., dan Fujii, K., 2017. Clinical and economic burdens experienced by patients with painful diabetic peripheral neuropathy : An observational study using a Japanese claims database. *PLoS ONE*, **12**: 1–13.

- Edwards, J.L., Vincent, A., Cheng, T., dan Feldman, E.L., 2008. Diabetic Neuropathy: Mechanisms to Management. *Pharmacology & Therapeutics*, **120**: 1–34.
- El-Akabawy, G. dan El-Kholy, W., 2014. Neuroprotective effect of ginger in the brain of streptozotocin-induced diabetic rats. *Annals of Anatomy*, **196**: 119–128.
- Fajrin, F.A., 2018. 'Mekanisme Molekular 6-shogaol pada Nyeri Neuropathy Diabetes (Painful Diabetic Neuropathy)', . Disertasi, Universitas Gadjah Mada, Yogyakarta.
- Fajrin, F.A., Nugroho, A.E., Nurrochmad, A., dan Susilowati, R., 2018. Molecular docking analysis of ginger active compound on transient receptor potential cation channel subfamily V member 1 (TRPV1). *Indonesian Journal of Chemistry*, **18**: 179–185.
- Fajrin, F.A., Nugroho, A.E., Nurrochmad, A., dan Susilowati, R., 2019a. Ginger extract and its compound, 6-shogaol, attenuates painful diabetic neuropathy in mice via reducing TRPV1 and NMDAR2B expressions in the spinal cord. *Journal of Ethnopharmacology*, 1–10.
- Fajrin, F.A., Nurrochmad, A., AE, N., dan Susilowati, R., 2017. Optimization of Mice Model of Painful Diabetic Neuropathy (PDN). *Journal of Medical Sciences*, **49**: 97–105.
- Fajrin, F.A., Nurrochmad, A., Nugroho, A.E., dan Susilowati, R., 2019b. The Improvement of Pain Behaviour and Sciatic Nerves Morphology in mice Model of Painful Diabetic Neuropathy upon Administration of Ginger (*Zingiber officinale* Roscoe.) Extract and Its Pungent Compound, 6-Shogaol. *Journal of Natural Science, Biology and Medicine*, **10**: 149–156.
- Fajrin, F.A. dan Purwandhono, A., 2016. 'Pengembangan minyak jahe (*Zingiber officinale*) sebagai pilihan terapi nyeri kronik pada keadaan

neuropati dan inflamasi', , *Laporan Akhir Penelitian Hibah Bersaing*, .
Universitas Negeri Jember, Jember.

Farmer, K.L., Li, C., dan Dobrowsky, R.T., 2012. Diabetic Peripheral Neuropathy: Should a Chaperone Accompany Our Therapeutic Approach? *Pharmacological Reviews*, **64**: 880–900.

Febriani, Y., Riasari, H., Winingsih, W., Aulifa, L., dan Permatasari, A., 2018. The Potential Use of Red Ginger (*Zingiber officinale* Roscoe) Dregs as Analgesic. *Indonesian Journal of Pharmaceutical Science and Technology Journal Homepage*, **1**: 57–64.

Feldman, E.L., Nave, K.A., Jensen, T.S., Bennett, D.L.H.H., Nave, K.A., dan Jensen, T.S., 2017. New Horizons in Diabetic Neuropathy: Mechanism, Bioenergetics, and Pain. *Neuron*, **93**: 1296–1313.

Fong, S.W., Lin, H.C., Wu, M.F., Chen, C.C., dan Huang, Y.S., 2016. CPEB3 deficiency elevates TRPV1 expression in dorsal root ganglia neurons to potentiate thermosensation. *PLoS ONE*, **11**: 1–12.

Frias, B. dan Merighi, A., 2016. Capsaicin, nociception and pain. *Molecules*, **21**: 1–33.

Furman, B.L., 2015. Streptozotocin-Induced Diabetic Models in Mice and Rats. *Current protocols in pharmacology*, **70**: 5.47.1-5.47.20.

Gandjar, I.G. dan Rohman, A., 2011. *Kimia Farmasi Analisis*, 1st ed. Pustaka Pelajar, Yogyakarta.

Gao, F. dan Zheng, Z.M., 2014. Animal models of diabetic neuropathic pain. *Experimental and Clinical Endocrinology and Diabetes*, **122**: 100–106.

Ghasemzadeh, A., Jaafar, H.Z.E., Baghdadi, A., dan Tayebi-Meigooni, A., 2018. Formation of 6-, 8- and 10-shogaol in ginger through application of different drying methods: Altered antioxidant and antimicrobial activity.

Molecules, **23**: 1–12.

Ghasemzadeh, A., Jaafar, H.Z.E., dan Rahmat, A., 2015. Optimization protocol for the extraction of 6-gingerol and 6-shogaol from *Zingiber officinale* var. *rubrum* Theilade and improving antioxidant and anticancer activity using response surface methodology. *BMC Complementary and Alternative Medicine*, **15**: 1–10.

Ghasemzadeh, A., Jaafar, H.Z.E., dan Rahmat, A., 2016. Variation of the phytochemical constituents and antioxidant activities of *Zingiber officinale* var. *rubrum* Theilade associated with different drying methods and polyphenol oxidase activity. *Molecules*, **21**: 1–12.

Girhepunje, N.S. dan Tilloo, S.K., 2016. Standardization of Some Bioactives in Ginger Extract. *Journal of Harmonized Research (JOHR)*, **5**: 86–94.

Gkogkolou, P. dan Böhm, M., 2012. Advanced glycation end products Key players in skin aging ? *Dermato-Endocrinology*, **4**: 259–270.

Goud, B.J., Dwarakanath, V., dan Chikka swamy, B.K., 2015. Streptozotocin - A Diabetogenic Agent in Animal Models. *International Journal of Pharmacy and Pharmaceutical Research. Human*, **3**: 253–269.

Graham, M.L., Janecek, J.L., Kittredge, J.A., Hering, B.J., dan Schuurman, H.J., 2011. The streptozotocin-induced diabetic nude mouse model: Differences between animals from different sources. *Comparative Medicine*, **61**: 356–360.

Grewal, A.S., Bhardwaj, S., Pandita, D., Lather, V., dan Sekhon, B.S., 2016. Updates on Aldose Reductase Inhibitors for Management of Diabetic Complications and Non-diabetic Diseases. *Mini-Reviews in Medicinal Chemistry*, **16**: 120–162.

- Groninger, H. dan Schisler, R.E., 2012. Fast Facts and Concepts Topical Capsaicin for Neuropathic Pain # 255. *Journal of Palliative Medicine*, **15**: 946–947.
- Gunduz, A., Eraydin, I., Turkmen, S., Kalkan, O.F., Turedi, S., Eryigit, U., dkk., 2014. Analgesic effects of mad honey (grayanotoxin) in mice models of acute pain and painful diabetic neuropathy. *Human and Experimental Toxicology*, **33**: 130–135.
- Gvazava, I.G., Rogovaya, O.S., Borisov, M.A., Vorotelyak, E.A., dan Vasiliev, A. V., 2018. Pathogenesis of type 1 diabetes mellitus and rodent experimental models. *Acta Naturae*, **10**: 24–33.
- Hariyadi, P., 2013. Freeze Drying Technology :for Better Quality & Flavor of Dried Products. *Foodreview Indonesia*, **VIII**: 52–57.
- Ho, E.C.M.M., Lam, K.S.L.L., Chen, Y.S., Yip, J.C.W.W., Arvindakshan, M., Yamagishi, S.-I.S.I., dkk., 2006. Aldose reductase-deficient mice are protected from delayed motor nerve conduction velocity, increased c-Jun NH2-terminal kinase activation, depletion of reduced glutathione, increased superoxide accumulation, and DNA damage. *Diabetes*, **55**: 1946–1953.
- Huang, J., Zhang, X., dan McNaughton, P., 2006. Inflammatory Pain: The Cellular Basis of Heat Hyperalgesia. *Current Neuropharmacology*, **4**: 197–206.
- Huang, T.C., Chung, C.C., Wang, H.Y., Law, C.L., dan Chen, H.H., 2011. Formation of 6-shogaol of ginger oil under different drying conditions. *Drying Technology*, **29**: 1884–1889.
- Hwang, S.W., Cho, H., Kwak, J., Lee, S.Y., Kang, C.J., Jung, J., dkk., 2000. Direct activation of capsaicin receptors by products of lipoxygenases: endogenous capsaicin-like substances. *Proc Natl Acad Sci U S A*, **97**:

6155–6160.

Indrawati, A., 2017. 'Teknik Pembuatan dan Evaluasi Preparat Histologi dengan Pewarnaan Hematoksin Eosin di Laboratorium Histologi dan Biologi Sel Fakultas Kedokteran UGM dan National Laboratory Animal Center (NLAC) Mahidol University', . SV UGM Yogyakarta.

INSTITUTE OF MEDICINE Committee on Pain, Disability, and C.I.B., 1992. The Anatomy and Physiology of Pain, dalam: Osterweis, M., Kleinman, A., dan Mechanic, D. (Editor), *Pain and Disability: Clinical, Behavioral, and Public Policy Perspectives*. National Academy of Sciences, Washington DC, hal. 123–145.

International Diabetes Federation, 2015. *IDF Diabetes Atlas*, 7th ed, International Diabetes Federation. International Diabetes Federation, Brussels.

Iqbal, Z., Azmi, S., Yadav, R., Ferdousi, M., Kumar, M., Cuthbertson, D.J., dkk., 2018. Diabetic Peripheral Neuropathy : Epidemiology, Diagnosis, and Pharmacotherapy. *Clinical Therapeutics*, **40**: 828–849.

Jara-Oseguera, A., Simon, S.A., dan Rosenbaum, T., 2008. TRPV1: on the road to pain relief. *Current molecular pharmacology*, **1**: 255–69.

Javed, S., Petropoulos, I.N., Alam, U., dan Malik, R.A., 2015. Treatment of painful diabetic neuropathy. *Therapeutic Advances in Chronic Disease*, **6**: 15–28.

Jung, M.Y., Lee, M.K., Park, H.J., Oh, E.B., Shin, J.Y., Park, J.S., dkk., 2018. Heat-induced conversion of gingerols to shogaols in ginger as affected by heat type (dry or moist heat), sample type (fresh or dried), temperature and time. *Food Science and Biotechnology*, **27**: 687–693.

Kammerman, 2016. Gabapentin for Neuropathic Pain External reviewers.

International Association for the Study of Pain, **1**: 16–20.

Kanai, Y., Hara, T., Imai, A., dan Sakakibara, A., 2007. Differential involvement of TRPV1 receptors at the central and peripheral nerves in CFA-induced mechanical and thermal hyperalgesia. *Journal of Pharmacy and Pharmacology*, **59**: 733–738.

Kandel, E.R., Schwartz, J.H., dan Jessell, T.M., 1991. *Principles of Neural Sciences*, 3rd ed. Appleton & Lange, Norwalk.

Kandhare, A.D., Raygude, K.S., Ghosh, P., Ghule, A.E., dan Bodhankar, S.L., 2012. Neuroprotective effect of naringin by modulation of endogenous biomarkers in streptozotocin induced painful diabetic neuropathy. *Fitoterapia*, **83**: 650–659.

Kato, A., Higuchi, Y., Goto, H., Kizu, H., Okamoto, T., Asano, N., dkk., 2006. Inhibitory effects of *Zingiber officinale* Roscoe derived components on aldose reductase activity in vitro and in vivo. *J Agric Food Chem*, **54**: 6640–6644.

Kee, Z., Kodji, X., dan Brain, S.D., 2018. The role of calcitonin gene related peptide (CGRP) in neurogenic vasodilation and its cardioprotective effects. *Frontiers in Physiology*, **9**: 1–13.

Kementerian Kesehatan Republik Indonesia, 2013. 'Situasi dan Analisis Diabetes', . Jakarta.

Khan, M.S.A. dan Ahmad, I., 2019. *Herbal Medicine: Current Trends and Future Prospects*, New Look to Phytomedicine. Elsevier Inc.

Khandouzi, N., Shidfar, F., Rajab, A., Rahideh, T., Hosseini, P., dan Taheri, M.M., 2015. The Effects of Ginger on Fasting Blood Sugar, Hemoglobin A1c, Apolipoprotein B, Apolipoprotein A-I and Malondialdehyde in Type 2 Diabetic Patients. *Iranian Journal of Pharmaceutical Research*, **14**:

131–140.

Kim, Y.S., Chu, Y., Han, L., Li, M., Li, Z., LaVinka, P.C., dkk., 2014. Central terminal sensitization of TRPV1 by descending serotonergic facilitation modulates chronic pain. *Neuron*, **81**: 873–887.

King, A.J.F., 2012. The use of animal models in diabetes research. *British Journal of Pharmacology*, **166**: 877–894.

Ko, M.J., Nam, H.H., dan Chung, M.S., 2019. Conversion of 6-gingerol to 6-shogaol in ginger (*Zingiber officinale*) pulp and peel during subcritical water extraction. *Food Chemistry*, **270**: 149–155.

Kuhad, A., Sharma, S., dan Chopra, K., 2008. Lycopene attenuates thermal hyperalgesia in a diabetic mouse model of neuropathic pain. *European Journal of Pain*, **12**: 624–632.

Kumar Gupta, S. dan Sharma, A., 2014. Medicinal properties of *Zingiber officinale* Roscoe-A Review. *IOSR Journal of Pharmacy and Biological Sciences*, **9**: 124–129.

Kurniasari, L., Hartati, I., dan Ratnani, R., 2008. Kajian Ekstraksi Minyak Jahe Menggunakan Microwave Assisted Extraction (Mae). *Momentum*, **4**: 47–52.

Kusumawati, N., Anggarani, M.A., Setiarso, P., dan Muslim, S., 2017. Product Standarization of Ginger (*Zingiber officinale* Rosc.) and Reg Ginger (*Zingiber officinale* var. *Rubrum*) Simplicia through Washing Time, Slice Thickness and Raw Materials Drying Process Optimization. *International Journal on Advanced Science Engineering Information Technology*, **7**: 15–21.

Kwon, N.S., Lee, S.H., Choi, C.S., Kho, T., dan Lee, H.S., 1994. Nitric oxide generation from streptozotocin. *FASEB journal : official publication of*

the Federation of American Societies for Experimental Biology, **8**: 529–533.

Layzell, M., 2008. Current interventions and approaches to postoperative pain management. *British Journal of Nursing*, **17**: 414–419.

Le May, C., Chu, K., Hu, M., Ortega, C.S., Simpson, E.R., Korach, K.S., dkk., 2006. Estrogens protect pancreatic beta-cells from apoptosis and prevent insulin-deficient diabetes mellitus in mice. *Proceedings of the National Academy of Sciences*, **103**: 9232–9237.

Lehning, E.J. dan Lopachin, R.M., 1994. Changes in Na⁺-K⁺ ATPase and protein kinase C activities in peripheral nerve of acrylamide-treated rats. *Journal of Toxicology and Environmental Health*, **42**: 331–342.

Lenzen, S., 2008. The mechanisms of alloxan- and streptozotocin-induced diabetes. *Diabetologia*, **51**: 216–226.

Li, L.L., Cui, Y., Guo, X.H., Ma, K., Tian, P., Feng, J., dkk., 2019. Pharmacokinetics and tissue distribution of gingerols and shogaols from ginger (*Zingiber officinale* Rosc.) in rats by UPLC–Q-Exactive–HRMS. *Molecules*, **24**: 1–12.

Li, X.H.H., McGrath, K.C.-Y.Y., Nammi, S., Heather, A.K., dan Roufogalis, B.D., 2012. Attenuation of Liver Pro-Inflammatory Responses by *Zingiber officinale* via Inhibition of NF- κ B Activation in High-Fat Diet-Fed Rats. *Basic and Clinical Pharmacology and Toxicology*, **110**: 238–244.

Li, Y., Tran, V.H., Duke, C.C., dan Roufogalis, B.D., 2012. Gingerols of *Zingiber officinale* enhance glucose uptake by increasing cell surface GLUT4 in cultured L6 myotubes. *Planta Medica*, **78**: 1549–1555.

Lim, T.K., 2016. *Edible Medicinal and Non-Medicinal Plants*, 1st ed, Edible

Medicinal and Non-Medicinal Plants. Springer Netherlands, Canberra.

Liu, S. dan Mauvais-Jarvis, F., 2009. Rapid, nongenomic estrogen actions protect pancreatic islet survival. *Islets*, **1**: 273–275.

Lozano, I., Werf, R. Van Der, Bietiger, W., Seyfritz, E., Peronet, C., Pinget, M., dkk., 2016. High-fructose and high-fat diet-induced disorders in rats: impact on diabetes risk, hepatic and vascular complications. *Nutrition & Metabolism*, **13**: 1–13.

Madkor, H.R., Mansour, S.W., dan Ramadan, G., 2011. Modulatory effects of garlic, ginger, turmeric and their mixture on hyperglycaemia, dyslipidaemia and oxidative stress in streptozotocin–nicotinamide diabetic rats. *British Journal of Nutrition*, **105**: 1210–1217.

Madonna, R. dan De Caterina, R., 2011. Cellular and molecular mechanisms of vascular injury in diabetes - Part I: Pathways of vascular disease in diabetes. *Vascular Pharmacology*, **54**: 68–74.

Marshall, S., Bacote, V., dan Traxinger, R.R., 1991. Discovery of a metabolic pathway mediating glucose-induced desensitization of the glucose transport system: role of hexosamine in the induction of insulin resistance. *Journal of Biological Chemistry*, **266**: 4706–4712.

McCarty, M.F., DiNicolantonio, J.J., dan O’Keefe, J.H., 2015. Capsaicin may have important potential for promoting vascular and metabolic health: Table 1. *Open Heart*, **2**: 1–7.

McEntire, D.M., Kirkpatrick, D.R., Dueck, N.P., Kerfeld, M.J., Smith, T.A., Nelson, T.J., dkk., 2016. Pain transduction: a pharmacologic perspective. *Expert Review of Clinical Pharmacology*, **9**: 1069–1080.

Melianita, F., Cholifah, S., Sumarlik, E., Kartinasari, W.F., dan Indrayanto, G., 2007. Simultaneous densitometric determination of 6-gingerol and 6-

shogaol in some commercial gingers (*Zingiber officinale* Roscoe). *Journal of Liquid Chromatography and Related Technologies*, **30**: 2941–2951.

Mesomo, M.C., Corazza, M.L., Ndiaye, P.M., Dalla Santa, O.R., Cardozo, L., dan Scheer, A.D.P., 2013. Supercritical CO₂ extracts and essential oil of ginger (*Zingiber officinale* R.): Chemical composition and antibacterial activity. *Journal of Supercritical Fluids*, **80**: 44–49.

Micov, A., Tomić, M., Pecikoza, U., Ugrešić, N., dan Stepanović-Petrović, R., 2015. Levetiracetam synergises with common analgesics in producing antinociception in a mouse model of painful diabetic neuropathy. *Pharmacological Research*, **97**: 131–142.

Montserrat-de la Paz, S., Garcia-Gimenez, M.D., Quilez, A.M., De la Puerta, R., dan Fernandez-Arche, A., 2018. Ginger rhizome enhances the anti-inflammatory and anti-nociceptive effects of paracetamol in an experimental mouse model of fibromyalgia. *Inflammopharmacology*, **26**: 1093–1101.

Morera, E., De Petrocellis, L., Morera, L., Moriello, A.S., Nalli, M., Di Marzo, V., dkk., 2012. Synthesis and biological evaluation of [6]-gingerol analogues as transient receptor potential channel TRPV1 and TRPA1 modulators. *Bioorganic and Medicinal Chemistry Letters*, **22**: 1674–1677.

Morrow, T.J., 2004. Animal Models of Painful Diabetic Neuropathy: The STZ Rat Model. *Current Protocols in Neuroscience*, **9**: 1–11.

Mukkavilli, R., Yang, C., Tanwar, R.S., Ghareeb, A., Luthra, L., dan Aneja, R., 2017. Absorption, metabolic stability, & pharmacokinetics of ginger phytochemicals. *Molecules*, **22**: 1–13.

Mulder, G.U.Y.B. dan Pritchett, K., 2004. Rodent Analgesiometry: The Hot Plate, Tail Flick and Von Frey Hairs **43**: 54–55.

- Nair, A. dan Jacob, S., 2016. A simple practice guide for dose conversion between animals and human. *Journal of Basic and Clinical Pharmacy*, **7**: 27–31.
- Nammi, S., Kim, M.S., Gavande, N.S., Li, G.Q., dan Roufogalis, B.D., 2010. Regulation of low-density lipoprotein receptor and 3-hydroxy-3-methylglutaryl coenzyme A reductase expression by zingiber officinale in the liver of high-fat diet-fed rats. *Basic and Clinical Pharmacology and Toxicology*, **106**: 389–395.
- Napitupulu, R., Wicaksono, L.S., Efizal, Mooduto, L., Herawaty, T., Novianti, A., dkk., 2008. *Taksonomi Koleksi Tanaman Obat Kebun Obat Citeureup*. Badan Pengawas Obat dan Makanan Republik Indonesia, Jakarta.
- National Center for Biotechnology Information, 2019. 'Streptozotocin', *PubChem Compound Database*. URL: <https://pubchem.ncbi.nlm.nih.gov/compound/Streptozotocin> (diakses tanggal 30/8/2019).
- Nesti, D.R., 2015. 'Morfologi, Morfometri dan Distribusi Sel Imunoreaktif Insulin dan Glukagon Pada Pankreas Tikus (*Rattus norvegicus*) Obesitas', . Tesis, M.Sc., Fakultas Kedokteran Hewan, Universitas Gadjah Mada, Yogyakarta.
- Nilius, B., Owsianik, G., Voets, T., dan Peters, J.A., 2007. Transient Receptor Potential Cation Channels in Disease. *Physiological Reviews*, **87**: 165–217.
- Nishikawa, T., Edelstein, D., Du, X.L., Yamagishi, S.I., Matsumura, T., Kaneda, Y., dkk., 2000. Normalizing mitochondrial superoxide production blocks three pathways of hyperglycaemic damage. *Nature*, **404**: 787–790.
- Nørgaard, S.A., Sand, F.W., Sørensen, D.B., Abelson, K.S.P., dan Søndergaard, H., 2018. Softened food reduces weight loss in the

streptozotocin-induced male mouse model of diabetic nephropathy.

Laboratory Animals, **52**: 373–383.

Novaes, R.D. dan Gonçalves, R.V., 2015. Comment on “The Combined Extract of *Zingiber officinale* and *Zea mays* (Purple Color) Improves Neuropathy, Oxidative Stress, and Axon Density in Streptozotocin Induced Diabetic Rats.” *Evidence-Based Complementary and Alternative Medicine*, **2015**: 1–2.

Numan, E.M., Jyad, J.S., Alazawi, A.H.I., Al-Jumaily, E.F., Jwad, A., Zehrawo, N., dkk., 2016. Comparison of Different Extraction Methods of (*Zingiber officinale*) on Chemical Composition, Antioxidant Activity. *International Journal of Pharmacy and Pharmaceutical Research*, **5**: 215–223.

O’Brien, P.D., Sakowski, S.A., dan Feldman, E.L., 2014. Mouse models of diabetic neuropathy. *ILAR Journal*, **54**: 259–272.

Obrosova, I.G., 2009. Diabetes and the peripheral nerve. *Biochimica et Biophysica Acta - Molecular Basis of Disease*, **1792**: 931–940.

Obrosova, I.G., Drel, V.R., Pacher, P., Ilnytska, O., Wang, Z.Q., Stevens, M.J., dkk., 2005. Oxidative-nitrosative stress and poly(ADP-ribose) polymerase (PARP) activation in experimental diabetic neuropathy: The relation is revisited. *Diabetes*, **54**: 3435–3441.

Oh, C.M., Park, S., dan Kim, H., 2016. Serotonin as a new therapeutic target for diabetes mellitus and obesity. *Diabetes and Metabolism Journal*, **40**: 89–98.

Ohbuchi, K., Mori, Y., Ogawa, K., Warabi, E., Yamamoto, M., dan Hirokawa, T., 2016. Detailed analysis of the binding mode of vanilloids to transient receptor potential vanilloid type I (TRPV1) by a mutational and computational study. *PLoS ONE*, **11**: 1–20.

- Ojewole, J.A.O., 2006. Analgesic, antiinflammatory and hypoglycaemic effects of ethanol extract of *Zingiber officinale* (roscoe) rhizomes (zingiberaceae) in mice and rats. *Phytotherapy Research*, **20**: 764–772.
- Ok, S. dan Jeong, W.S., 2012. Optimization of extraction conditions for the 6-shogaol-rich extract from ginger (*Zingiber officinale* Roscoe). *Preventive Nutrition and Food Science*, **17**: 166–171.
- Ozcan, M., Ayar, A., Canpolat, S., dan Kutlu, S., 2008. Antinociceptive efficacy of levetiracetam in a mice model for painful diabetic neuropathy. *Acta Anaesthesiologica Scandinavica*, **52**: 926–930.
- Pabbidi, R.M., Yu, S.Q., Peng, S., Khardori, R., Pauza, M.E., dan Premkumar, L.S., 2008. Influence of TRPV1 on diabetes-induced alterations in thermal pain sensitivity. *Molecular Pain*, **4**: 1–17.
- Pacher, P. dan Szabo, C., 2008. Role of the peroxynitrite-poly(ADP-ribose) polymerase pathway in human disease. *American Journal of Pathology*, **173**: 2–13.
- Paoletti, P. dan Neyton, J., 2007. NMDA receptor subunits: function and pharmacology. *Current Opinion in Pharmacology*, **7**: 39–47.
- Peng, H.-Y., Chang, H.-M., Lee, S.-D., Huang, P.-C., Chen, G.-D., Lai, C.-H.C.-Y., dkk., 2008. TRPV1 mediates the uterine capsaicin-induced NMDA NR2B-dependent cross-organ reflex sensitization in anesthetized rats. *American journal of physiology. Renal physiology*, **295**: 1324–1335.
- Peppas, M., Uribarri, J., dan Vlassara, H., 2003. Glucose, Advanced Glycation End Products, and Diabetes Complications: What Is New and What Works. *Clinical Diabetes*, **21**: 186–187.
- Philippaert, K. dan Vennekens, R., 2015. Transient Receptor Potential (TRP) Cation Channels in Diabetes, dalam: Szallasi, A. (Editor), *TRP Channels*

as Therapeutic Targets: From Basic Science to Clinical Use. Academic Press, San Diego, USA, hal. 343–363.

Premkumar, L.S., 2014. Transient receptor potential channels as targets for phytochemicals. *ACS Chemical Neuroscience*, **5**: 1117–1130.

Premkumar, L.S. dan Bishnoi, M., 2011. Disease-Related Changes in TRPV1 Expression and Its Implications for Drug Development. *Current Topics in Medicinal Chemistry*, **11**: 2192–2209.

Prosek, M. dan Vovk, I., 2003. Basic Principles of Optical Quantification in TLC, dalam: Sherma, J. dan Fried, B. (Editor), *Handbook of Thin-Layer Chromatography*. Marcel Dekker, Inc., New York Basel, hal. 277–306.

Purves, D., Augustine, G.J., Fitzpatrick, D., Hall, W.C., Lamantia, A.-S., McNamara, J.O., dkk. (Editor), 2004. *Neuroscience*, 3rd ed. Sinauer Associates, Inc., Sunderland, Massachusetts USA.

Putri, D.A., Daulay, S.B., dan Rindang, A., 2018. Uji Pengaruh Kondisi Bahan dan Lama Waktu Penyulingan Pada Alat Penyuling Tipe Uap dan Air terhadap Rendemen Minyak Atsiri Tanaman Kencur (*Kaempferia Galanga* , L). *Jurnal Rekayasa Pangan dan Pertanian*, **6**: 154–160.

Qasim, M., 2011. Hypoglycemic Effect of Ginger (*Zingiber officinale*) in Alloxan Induced Diabetic Rats (*Rattus norvegicus*). *Pakistan Veterinary Journal*, **31**: 160–162.

Quintero, G.C., 2017. Review about gabapentin misuse, interactions, contraindications and side effects. *Journal of Experimental Pharmacology*, **9**: 13–21.

Rahmadani, S., Sa'diah, S., dan Wardatun, S., 2018. Optimasi ekstraksi jahe merah (*Zingiber officinale* Roscoe) dengan Metode Maserasi. *Jurnal Online Mahasiswa (JOM) Bidang Farmasi*, **1**: 10.

- Rai, S., Mukherjee, K., Mal, M., Wahile, A., Saha, B.P., dan Mukherjee, P.K., 2006. Determination of 6-gingerol in ginger (*Zingiber officinale*) using high-performance thin-layer chromatography. *Journal of Separation Science*, **29**: 2292–2295.
- Rajan, R.S., Gray, L. de, dan George, E., 2014. Painful diabetic neuropathy. *Continuing Education in Anaesthesia Critical Care & Pain*, **14**: 230–235.
- Ramer, L.M., Peter van Stolk, A., Inskip, J.A., Ramer, M.S., dan Krassioukov, A. V., 2012. Plasticity of trpv1-expressing sensory neurons mediating autonomic dysreflexia following spinal cord injury. *Frontiers in Physiology*, **3**: 1–16.
- Ramudu, S.K., Korivi, M., Kesireddy, N., Lee, L.C., Cheng, I.S., Kuo, C.H., dkk., 2011. Nephro-protective effects of a ginger extract on cytosolic and mitochondrial enzymes against streptozotocin (STZ)-induced diabetic complications in rats. *Chinese Journal of Physiology*, **54**: 79–86.
- Reddy, D.S., 2019. An enigmatic role of tonic inhibition in gabapentin therapy. *EBioMedicine*, **42**: 14–15.
- Richner, M., Jager, S.B., Siupka, P., dan Vaegter, C.B., 2017. Hydraulic Extrusion of the Spinal Cord and Isolation of Dorsal Root Ganglia in Rodents. *Journal of Visualized Experiments*, **119**: 1–6.
- Riera, C.E., Menozzi-Smarrito, C., Affolter, M., Michlig, S., Munari, C., Robert, F., dkk., 2009. Compounds from Sichuan and Melegueta peppers activate, covalently and non-covalently, TRPA1 and TRPV1 channels. *British Journal of Pharmacology*, **157**: 1398–1409.
- Rodriguez, L., 2015. Pathophysiology of pain: Implications for perioperative nursing. *AORN Journal*, **101**: 338–344.
- Rosenbaum, T. dan Simon, S.A., 2007. TRPV1 Receptors and Signal

Transduction, dalam: WB, L. dan S, H. (Editor), *TRP Ion Channel Function in Sensory Transduction and Cellular Signaling Cascades*. Taylor & Francis Group, Boca Raton (Florida).

Sallum, A.M.C., Garcia, D.M., dan Sanches, M., 2012. Acute and chronic pain: a narrative review of the literature. *Acta Paulista de Enfermagem*, **25**: 150–154.

Salmon, C.N.A., Bailey-Shaw, Y.A., Hibbert, S., Green, C., Smith, A.M., dan Williams, L.A.D., 2012. Characterisation of cultivars of Jamaican ginger (*Zingiber officinale* Roscoe) by HPTLC and HPLC. *Food Chemistry*, **131**: 1517–1522.

Sampath, C., Rashid, M.R., Sang, S., dan Ahmedna, M., 2017. Specific bioactive compounds in ginger and apple alleviate hyperglycemia in mice with high fat diet-induced obesity via Nrf2 mediated pathway. *Food Chemistry*, **226**: 79–88.

Santiago, M. dan Strobel, S., 2013. Thin layer chromatography, dalam: Lorsch, J. (Editor), *Laboratory Methods in Enzymology: Cell, Lipid and Carbohydrate*. Academic Press, San Diego, USA, hal. 303–324.

Santos-Nogueira, E., Redondo Castro, E., Mancuso, R., dan Navarro, X., 2012. Randall-Selitto Test: A New Approach for the Detection of Neuropathic Pain after Spinal Cord Injury. *Journal of Neurotrauma*, **29**: 898–904.

Santos-Sánchez, N.F., Salas-Coronado, R., Valadez-Blanco, R., Hernández-Carlos, B., dan Guadarrama-Mendoza, P.C., 2017. Natural antioxidant extracts as food preservatives. *Acta Scientiarum Polonorum, Technologia Alimentaria*, **16**: 361–370.

Sanz-Salvador, L., Andrés-Borderia, A., Ferrer-Montiel, A., dan Planells-Cases, R., 2012. Agonist- and Ca²⁺-dependent desensitization of TRPV1 channel targets the receptor to lysosomes for degradation. *Journal of*

Biological Chemistry, **287**: 19462–19471.

Saraswat, M., Reddy, P.Y., Muthenna, P., dan Reddy, G.B., 2009. Prevention of non-enzymic glycation of proteins by dietary agents: prospects for alleviating diabetic complications. *The British Journal of Nutrition*, **101**: 1714–1721.

Saraswat, M., Suryanarayana, P., Reddy, P.Y., Patil, M.A., Balakrishna, N., dan Reddy, G.B., 2010. Antiglycating potential of *Zingiber officinalis* and delay of diabetic cataract in rats. *Molecular vision*, **16**: 1525–1537.

Sekiya, K., Ohtani, A., dan Kusano, S., 2004. Enhancement of insulin sensitivity in adipocytes by ginger. *BioFactors*, **22**: 153–156.

Semwal, R.B., Semwal, D.K., Combrinck, S., dan Viljoen, A.M., 2015. Gingerols and shogaols: Important nutraceutical principles from ginger. *Phytochemistry*, **117**: 554–568.

Setiawan, I.M., 2013. 'Efek Antidiabetes Kombinasi Ekstrak Terpurifikasi Herba Sambiloto (*Andrographis paniculata* (Burm.f.) Nees) dan Glibenklamid pada Tikus Diabetes Mellitus tipe 2 Defisiensi Insulin', , *Tesis*, . M.Sc., Fakultas Farmasi, Universitas Gadjah Mada, Yogyakarta.

Shaikh, A.S. dan Somani, R.S., 2010. Animal models and biomarkers of neuropathy in diabetic rodents. *Indian Journal of Pharmacology*, **42**: 129–134.

Shanmugam, K.R., Mallikarjuna, K., Kesireddy, N., dan Sathyavelu Reddy, K., 2011a. Neuroprotective effect of ginger on anti-oxidant enzymes in streptozotocin-induced diabetic rats. *Food and Chemical Toxicology*, **49**: 893–897.

Shanmugam, K.R., Mallikarjuna, K., Nishanth, K., Kuo, C.H., dan Reddy, K.S., 2011b. Protective effect of dietary ginger on antioxidant enzymes

and oxidative damage in experimental diabetic rat tissues. *Food Chemistry*, **124**: 1436–1442.

Shanmugam, K.R., Ramakrishna, C.H., Mallikarjuna, K., Reddy, K.S., Ramakrishana, C., Mallikarjuna, K., dkk., 2009. The Impact of Ginger on Kidney Carbohydrate Metabolic Profiles in STZ Induced Diabetic Rats. *Asian J. Exp. Sci*, **23**: 127–134.

Sharif, M.F. dan Bennett, M.T., 2016. The Effect of Different Methods and Solvents on the Extraction of Polyphenols in Ginger (*Zingiber officinale*). *Jurnal Teknologi*, **78**: 49–54.

Sharma, S., Kulkarni, S.K., dan Chopra, K., 2007. Effect of resveratrol, a polyphenolic phytoalexin, on thermal hyperalgesia in a mouse model of diabetic neuropathic pain. *Fundamental and Clinical Pharmacology*, **21**: 89–94.

Shimoda, H., Shan, S.-J., Tanaka, J., Seki, A., Seo, J.-W., Kasajima, N., dkk., 2010. Anti-inflammatory properties of red ginger (*Zingiber officinale* var. *Rubra*) extract and suppression of nitric oxide production by its constituents. *Journal of medicinal food*, **13**: 156–162.

Singh, R., Kishore, L., dan Kaur, N., 2014. Diabetic peripheral neuropathy: Current perspective and future directions. *Pharmacological Research*, **80**: 21–35.

Soboleva, A., Mavropulo-Stolyarenko, G., Karonova, T., Thieme, D., Hoehenwarter, W., Ihling, C., dkk., 2019. Multiple Glycation Sites in Blood Plasma Proteins as an Integrated Biomarker of Type 2 Diabetes Mellitus. *International Journal of Molecular Sciences*, **20**: 1–25.

Son, M.J., Miura, Y., dan Yagasaki, K., 2015. Mechanisms for antidiabetic effect of gingerol in cultured cells and obese diabetic model mice. *Cytotechnology*, **67**: 641–652.

- Spiegel, B.M.R., Khanna, D., Bolus, R., Agarwal, N., Khanna, P., dan Chang, L., 2011. Understanding Gastrointestinal Distress: A Framework for Clinical Practice. *American Journal of Gastroenterology*, **106**: 380–385.
- Stanisiere, J., Mousset, P.Y., dan Lafay, S., 2018. How safe is ginger rhizome for decreasing nausea and vomiting in women during early pregnancy? *Foods*, **7**: 1–29.
- Steeds, C.E., 2016. The anatomy and physiology of pain. *Surgery*, **34**: 55–59.
- Sukalingam, K., Ganesan, K., dan Gani, S.B., 2019. Hypoglycemic Effect of 6-Gingerol , an Active Principle of Ginger in Research and Reviews : Journal of Pharmacology and Toxicological Studies. *Journal of Pharmacology and Toxicological Studies*, **1**: 33–37.
- Supardan, M.D., Fuadi, A., Alam, P.N., dan Arpi, N., 2012. Solvent Extraction of Ginger Oleoresin Using Ultrasound. *MAKARA of Science Series*, **15**: 163–167.
- Suzuki, Y., Goto, K., Ishige, A., Komatsu, Y., dan Kamei, J., 1999. Antinociceptive effect of Gosha-jinki-gan, a Kampo medicine, in streptozotocin-induced diabetic mice. *Japanese Journal of Pharmacology*, **79**: 169–175.
- Sytze Van Dam, P., Cotter, M.A., Bravenboer, B., dan Cameron, N.E., 2013. Pathogenesis of diabetic neuropathy: Focus on neurovascular mechanisms. *European Journal of Pharmacology*, **719**: 180–186.
- Szkudelski, T., 2001. The mechanism of alloxan and streptozotocin action in B cells of the rat pancreas. *Physiological Research*, **50**: 537–546.
- Tay, Y.C., Wang, Y., Kairaitis, L., Rangan, G.K., Zhang, C., dan Harris, D.C.H., 2005. Can murine diabetic nephropathy be separated from superimposed acute renal failure? *Kidney International*, **68**: 391–398.

Tesfaye, S., Boulton, A.J.M., Dyck, P.J., Freeman, R., Horowitz, M., Kempler, P., dkk., 2010. Diabetic neuropathies: Update on definitions, diagnostic criteria, estimation of severity, and treatments. *Diabetes Care*, **33**: 2285–2293.

Tomić, M.A., Vučković, S.M., Stepanović-Petrović, R.M., Micov, A.M., Ugrešić, N.D., Prostran, M.Š., dkk., 2010. Analysis of the antinociceptive interactions in two-drug combinations of gabapentin, oxcarbazepine and amitriptyline in streptozotocin-induced diabetic mice. *European Journal of Pharmacology*, **628**: 75–82.

Vincent, A.M., Callaghan, B.C., Smith, A.L., dan Feldman, E.L., 2011. Diabetic neuropathy: cellular mechanisms as therapeutic targets. *Nature Reviews Neurology*, **7**: 573–583.

Vincent, A.M., Perrone, L., Sullivan, K.A., Backus, C., Sastry, A.M., Lastoskie, C., dkk., 2007. Receptor for advanced glycation end products activation injures primary sensory neurons via oxidative stress. *Endocrinology*, **148**: 548–558.

Visnagri, A., Kandhare, A.D., Chakravarty, S., Ghosh, P., dan Bodhankar, S.L., 2014. Hesperidin, a flavanoglycone attenuates experimental diabetic neuropathy via modulation of cellular and biochemical marker to improve nerve functions. *Pharmaceutical Biology*, **52**: 814–828.

Vyklický, L., Nováková-Toušová, K., Benedikt, J., Samad, A., Touška, F., dan Vlachova, V., 2008. Calcium-dependent desensitization of vanilloid receptor TRPV1: A mechanism possibly involved in analgesia induced by topical application of capsaicin. *Physiological Research*, **57**: 1–10.

Wada, R. dan Yagihashi, S., 2005. Role of advanced glycation end products and their receptors in development of diabetic neuropathy. *Annals of the New York Academy of Sciences*, **1043**: 598–604.

- Waksmundzka-Hajnos, M., 2008. Thin-Layer Chromatography. *Journal of Chromatographic Science*, **46**: 289–290.
- Wattanathorn, J., Thiraphatthanavong, P., Muchimapura, S., Thukhammee, W., Lertrat, K., dan Suriharn, B., 2015. The combined extract of *Zingiber officinale* and *Zea mays* (purple color) improves neuropathy, oxidative stress, and axon density in streptozotocin induced diabetic rats. *Evidence-based Complementary and Alternative Medicine*, **2015**: 1–11.
- Wei, C.K., Tsai, Y.H., Korinek, M., Hung, P.H., El-Shazly, M., Cheng, Y. Bin, dkk., 2017. 6-Paradol and 6-Shogaol, the Pungent Compounds of Ginger, Promote Glucose Utilization in Adipocytes and Myotubes, and 6-Paradol Reduces Blood Glucose in High-Fat Diet-Fed Mice. *International Journal of Molecular Sciences*, **18**: 1–18.
- Wells, B.G., DiPiro, J.T., Matzke, G.R., Posey, L.M., dan Schwinghammer, T.L., 2009. *Pharmacotherapy Handbook (7th Edition)*. McGraw-Hill Professional Publishing, New York, USA.
- WHO, 1999. 'Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications', , *Report of a WHO Consultation*, , Part 1 : Diagnosis and Classification Diabetes Mellitus. Department of Noncommunicable Disease Surveillance World Health Organization, Geneva.
- World Health Organization, 2016. *Global Report on Diabetes*. WHO Press, World Health Organization, Geneva.
- Wu, J. dan Yan, L.J., 2015. Streptozotocin-induced type 1 diabetes in rodents as a model for studying mitochondrial mechanisms of diabetic β cell glucotoxicity. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy*, **8**: 181–188.
- Yang, F., Xiao, X., Cheng, W., Yang, W., Yu, P., Song, Z., dkk., 2015. Structural mechanism underlying capsaicin binding and activation of

TRPV1 ion channel. *Nature Chemical Biology*, **11**: 518–524.

Yang, F., Xiao, X., Lee, B.H., Vu, S., Yang, W., Yarov-Yarovoy, V., dkk., 2018. The conformational wave in capsaicin activation of transient receptor potential vanilloid 1 ion channel. *Nature Communications*, **9**: 1–9.

Yi, J.K., Ryoo, Z.Y., Ha, J.J., Oh, D.Y., Kim, M.O., dan Kim, S.H., 2019. Beneficial effects of 6-shogaol on hyperglycemia, islet morphology and apoptosis in some tissues of streptozotocin-induced diabetic mice. *Diabetology and Metabolic Syndrome*, **11**: 1–13.

Yin, Y., Dong, Y., Vu, S., Yang, F., Yarov-Yarovoy, V., Tian, Y., dkk., 2019. Structural mechanisms underlying activation of TRPV1 channels by pungent compounds in gingers. *British Journal of Pharmacology*, **176**: 3364–3377.

You, H., Ireland, B., Moeszinger, M., Zhang, H., Snow, L., Krepich, S., dkk., 2019. Determination of bioactive nonvolatile ginger constituents in dietary supplements by a rapid and economic HPLC method: Analytical method development and single-laboratory validation. *Talanta*, **194**: 795–802.

Yue, H.Y., Jiang, C.Y., Fujita, T., dan Kumamoto, E., 2013. Zingerone enhances glutamatergic spontaneous excitatory transmission by activating TRPA1 but not TRPV1 channels in the adult rat substantia gelatinosa. *Journal of Neurophysiology*, **110**: 658–671.

Yuk, S.C., Chung, S.S.M., dan Chung, S.K., 2005. Noninvasive monitoring of diabetes-induced cutaneous nerve fiber loss and hypoalgesia in thy1-YFP transgenic mice. *Diabetes*, **54**: 3112–3118.

Zafar, M. dan Naeem-ul-Hassan Naqvi, S., 2010. Effects of STZ-Induced Diabetes on the Relative Weights of Kidney, Liver and Pancreas in Albino

Rats: A Comparative Study. *International Journal of Morphology*, **28**: 135–142.

Zhang, H., Wang, Q., Sun, C., Zhu, Y., Yang, Q., Wei, Q., dkk., 2019. Enhanced oral bioavailability, anti-tumor activity and hepatoprotective effect of 6-shogaol loaded in a type of novel micelles of polyethylene Glycol and Linoleic Acid Conjugate. *Pharmaceutics*, **11**: 1–16.

Zhou, H.-Y., Chen, S.-R., Chen, H., dan Pan, H.-L., 2009. The Glutamatergic Nature of TRPV1-Expressing Neurons in the Spinal Dorsal Horn. *Journal of Neurochemistry*, **108**: 305–318.

Ziegler, D., 2008. Painful diabetic neuropathy: treatment and future aspects. *Diabetes/Metabolism Research and Reviews*, **24**: 52–57.

Zychowska, M., Rojewska, E., Przewlocka, B., dan Mika, J., 2013. Mechanisms and pharmacology of diabetic neuropathy—experimental and clinical studies. *Pharmacological Reports*, **65**: 1601–1610.

Zygmunt, P.M., Petersson, J., Andersson, D.A., Chuang, H., Sjørgård, M., Di Marzo, V., dkk., 1999. Vanilloid receptors on sensory nerves mediate the vasodilator action of anandamide. *Nature*, **400**: 452.