THE EFFECT OF PROPOLIS TO AMOUNT OF PYRAMIDAL NEURON IN CORTEX PREFRONTALIS RAT (*Rattus novergicus*) INDUCED BY SODIUM NITRITE.

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Abstract

Statement of the problem : sodium nitrite is a compound highly used in the processing of food and drink especially as a food preservative. Excess consumption of sodium nitrite can cause hypoxia in the tissue because eritrosit fails to bind oxygen. Pyramidal neurons of prefrontal cortex are susceptible to hypoxia and can cause cell apoptosis. Neuroprotective agent is needed to prevent cell death due to sodium nitrite. Propolis is an agent with potent antioxidant ingredient and known as neuroprotective agent. Objective : this research aimed to know the effect of giving propolis on the number of the pyramidal neuron in prefrontal cortex of rat (Rattus novergicus) induced by sodium nitrite. Methods : this research is experiment using post-test with control group design. The subjects are rats (Rattus novergicus) divided into three groups, the control group induced by sodium nitrite 50 mg/kgBB/day , the treatment group 1 (P1) induced by sodium nitrite 50 mg/kgBB/day and given propolis 100 mg/kgBB/day , and the treatment group 2 (P2) induced by sodium nitrite 50 mg/kgBB/day and given propolis 200 mg/kgBB. Paraffin blocks were made into histologic preparations and stained by HE. The observational results was analyzed using one-way ANOVA and post-hoc test. Result : using one-way ANOVA, there is a significant difference of pyramidal neuron number in prefrontal cortex of rats between control group (K) , treatment group 1(P1), and treatment group 2 (P2) (p=0,002). In post-hoc test, there is significant difference between control group with treatment group 1 and treatment group 2. But there is no significant difference between treatment group 1 and treatment group 2. Conclusion : The given of Propolis prevent the reduction pyramidal neuron number in rat's prefrontal cortex induced by sodium nitrite.

Refference

Aliboni, A., D'Andrea, A. & Massanisso, P., 2011. Treatment of propolis specimens from Central Italy to yield a product with a lower charge of allergenic species. *Elsevier Separation and Purification Technology*, Volume 82, p. 71–75.

Alkis, H. et al., 2015. Neuroprotective effects of propolis and caffeic acid phenethyl ester (CAPE) on the radiation-injured brain tissue (Neuroprotective effects of propolis and CAPE). *International Journal of Radiation Research*, Volume 13.

Ambarwati, R., 2012. Effect of Sodium Nitrite (NaNO2) to Erithrocyte and Hemoglobin Profile in White Rats (Rattus norvegicus). *Folia Medica Indonesiana*, Volume 48.

Amin, R. A., Elsabagh, R. A. & Amin, A., 2016. Protective Effects of Ascorbic Acid and Garlic Oil against Toxic Effects induced by Sodium Nitrite as Meat Additive in Male Rats. *Global Veterinaria*, Volume 16, pp. 508-524.

Asni , E., Harahap, I., Prijanti, A., Wanandi, S., Jusman, S., & Sadikin, M. (2009). Pengaruh hipoksia berkelanjutan terhadap kadar malonaldehid, glutation tereduksi dan aktivitas katalase ginjal tikus. *Maj Kedokt Indon*, 595-600.

Aunapuu, M. & Arend, A., 2013. *University of Tartu, Morphology of Nervous System.*[Online] Available at: https://sisu.ut.ee/histology/cerebral-cortex [Accessed 5 October 2016].

Ayuningtias, S.H., 2015. Pengaruh Pemberian Ekstrak Ethanol Daun Pegagan (Centella asiatica) Terhadap Jumlah Neuron Piramidal CA1 Hipokampus Tikus (Rattus novergicus) yang Diinduksi Natrium Nitrit Sub Akut, Skripsi. Jurusan Pendidikan Dokter Fakultas Kedokteran, Universitas Islam Indonesia.

Badan Pengawas Obat Dan Makanan Republik Indonesia, 2013. *peraturan kepala badan pengawas obat dan makanan republik Indonesia no 36 tahun 2013 tentang batas maksimum penggunaan bahan tambahan pangan pengawet.* Jakarta: s.n.

Balakhrisnan, K. et al., 2015. Impact of amyloid beta aggregate maturation on antibody treatment in APP23 mice. *Acta Neuropathol*, 3(41).

Bak, J., Kim, H. J., Kim, S. Y., & Choi, Y.-S. (2016). Neuroprotective effect of caffeic acid phenethyl ester in 3-nitropropionic acid-induced striatal neurotoxicity. *Korean J Physiol Pharmacol*, 279-286.

Basarslan, S. K., Osun, A., Senol, S., Korkmaz, M., Ozkan, U., & Kaplan, I. (2016). Protective Effects of Intralipid and Caffeic Acid Phenyl Esther (CAPE) on Neurotoxicity Induced by Ethanol in Rats. *Turkish Neurosurgery*, 66-73.

Bhadauria, M., 2012. Combined treatment of HEDTA and propolis prevents aluminum induced toxicity in rats. *Elsevier Food and Chemical Toxicology*, Volume 50, p. 2487–2495.

Chan, P. C. et al., 2001. *Toxicology and Carcinogenesis Studies of Sodium.* s.l.:NIH Publication No. 01-3954.

Coutlee, C. G. & Huettel, S. A., 2011. The functional neuroanatomy of decision making: Prefrontal control of thought and action. *Elsevier*, pp. 3-12.

Daleprane, J. B. & Abdalla, D. S., 2013. Emerging roles of propolis: Antioxidant, cardioprotective, and antiangiogenic actions.. *Evidence-based Complementary and Alternative Medicine.*

Damayanti, R., Fitri, L.E. & Dalhar, M., 2016. Pengaruh Pemberian Propolis terhadap Ekspresi INOS dan Kadar MDA pada Otak Tikus Model Cedera Otak Traumatik. *Jurnal Kedokteran Brawijaya*, 29(2), pp.110–116.

Deshmukh, S. S. & Knierim, J. J., 2012. Hippocampus.. *Wiley Interdisciplinary Reviews: Cognitive Science*, Volume 3, pp. 231-251.

Doganyigit, Z., Kup, F. O., Silici, S., Deniz, K., Yakan, B., & Atayoglu, T. (2013). Protective effects of propolis on female rats histopathological, biochemical, and genotoxic changes during LPS induced endotoxemia. *Elsevier*, 632-639.

El-Masry, T. A., Emara, A. M. & El-Shitany, N. A., 2011. Possible protective effect of propolis against leadinduced neurotoxicity in animal model. *Journal of Evolutionary Biology Research*, Volume 3, pp. 4-11.

Eroschenko, V. P., 2010. *atlas histologi diFiore: dengan korelasi*. 11 ed. Jakarta: EGC.

Farooqui, T. & Farooqui, A. A., 2012. Beneficial effects of propolis on human health and neurological diseases.. *Frontiers in Bioscience.*, pp. 779-793.

Gehle, K., 2013. *ATSDR Case Studies in Environmental Medicine Nitrate/Nitrite.* s.l.:ATSDR, U.S. Departement of Health and Human Service.

Goldwater, D. S. et al., 2009. Structural and functional alterations to rat medial prefrontal cortex following chronic restraint stress and recovery. *NIH Public Access*, p. 798–808.

Gonzalez, M. T. N. D. et al., 2012. Survey of Residual Nitrite and Nitrate in Conventional and Organic/Natural/Uncured/Indirectly Cured Meats Available at Retail in the united states. *Journal of Agricultural and Food Chemistry*, pp. 3981-3990.

Guyton, A. C. & Hall, J. E., 2007. *Buku Ajar Fisiologi Kedokteran.* 11th ed. Jakarta: EGC.

Harper, C. et al., 2015. *draft toxicological profile for nitrate an nitrite*. Atlanta: U.S. Department of health and human services Public Health Service Agency for Toxic Substances and Disease Registry.

Helal, E., Zahkok, S., Soliman, G. Z. A. & Al-Kassas, M., 2008. Biochemical Studies On The Effect Of Sodium Nitrite And/Or Glutathione Treatment On Male Rats. *The Egyptian Journal of Hospital Medicine*, Volume 30, p. 25– 38.

Hidayat, A., Wiradisastra, K., Hernowo, B.S., Achmad, T.H., 2011. Ekspresi Bcl2 dan Caspase-3 Pasca Paparan Hipoksia Hipobarik Intermiten. Bandung Medical Journal. 43(4): 166-170.

Huang, S. et al., 2014. Recent Advances in the Chemical Composition of Propolis. *Molecules*, 19(12), pp.19610–19632. Available at: http://www.mdpi.com/1420-3049/19/12/19610/.

Ichwan, F. M., 2016. *Pengaruh pemberian propolis terhadap gambaran histopatologi renal pada tikus (Sprague dawley) yang diberi perlakuan stress isolasi sosial.*, Yogyakarta: Fakultas Kedokteran Universitas Islam Indonesia.

Kumar, V., Abbas, A. K. & Aster, J. C., 2013. *Buku Ajar Patologi Robbins.* 9th ed. singapore: Elsevier Saunders.

Kumar, V., Cotran, R. S. & Robbins, S. L., 2012. *Buku Ajar Patologi*. 7 ed. Jakarta: EGC.

Liang, G., Shi, B., Luo, W., & Yang, J. (2015). The protective effect of caffeic acid on global cerebral ischemia-reperfusion injury in rats. *Behavioral and Brain Functions*.

Lim, S.-c., Foster, N. .. & Riley, T. V., 2016. Susceptibility of Clostridium difficile to the food preservatives sodium. *Elsevier Ltd.*

Lundberg, J. O., Weitzberg, E. & Gladwin, M. T., 2008. The nitrate–nitrite–nitric oxide pathway in physiology and therapeutics. *Nature Reviews Drug Discovery,* Volume 7, pp. 156-167.

Lyhatskiy, P.G. et al., 2013. Methabolic Abnormalities in the Organism of Rats Under the Conditions of Sodium Nitrite Damage. SHEI. 434(615);1-9.

Menteri Kesehatan Republik Indonesia, 2013. *Peraturan Menteri Kesehatan Indonesia No.033 tahun 2013 Tentang Bahan Tambahan Pangan.*. s.l.:s.n.

Nabavi, S. F. et al., 2015. Neuroprotective effects of chrysin: From chemistry to medicine. *Elsevier Neurochemistry International,* Volume 90, pp. 224-231.

O'Reilly, R. C., 2010. The What and How of prefrontal. *Trends in Neurosciences,* Volume 33.

Petrova, E. B., DIshkelov , A. T. & Vasileva, E. G., 2011. Glycolipid changes in rat brain mitochondria ang synaptosomes following experimental hypoxia. *medicinska revija,* Volume 3, pp. 331-334.

Popova, M. et al., 2010. A validated spectrophotometric method for quantification of prenylated flavanones in pacific propolis from Taiwan. *Phytochemical Analysis*, 21(2), pp.186–191.

Pulungan, Z. S. A., Sofro, Z. M. & Partadiredja, G., 2016. Sodium fluoride does not affect the working memory and number of pyramidal cells in rat medial prefrontal cortex. *CrossMark,* Issue Japanese Association of Anatomists.

Safari, M., Sameni, H. R., Badban, L., Bandegi, A. R., Vafaei, A. A., Puor, A. R., & Ghahari, L. (2015). Protective Effects of Water Extract of Propolis on Dopaminergic Neurons, Brain Derived Neurotrophic Factor and stress Oxidative Factor in the rat model of parkinson's disease. *International Journal of Pharmacology*, 300-308.

Santoso, A. F., 2016. *Pengaruh Pemberian Ekstrak Etanol Pegagan (Centella asiatica) Terhadap Ekspresi Bax pada Neuron Pyramidal CA1 Hippocampus Tikus (Rattus novergicus) yang diinduksi Sodium Nitrit Sub Akut,* Yogyakarta: Fakultas Kedokteran Universitas Islam Indonesia.

Sforcin, J. M. & Bankova, V., 2011. Propolis: Is there a potential for the development on new drugs?. *Journal of Ethnopharmacology,* pp. 253-260.

Sherwood, L., 2012. *Fisiologi Manusia dari Sel ke Sistem.*. 6 ed. Jakarta: EGC.

Speijers, G. & Brandt, P., 2014. *Nitrite and potential endogenous formation of N-nitroso compounds.*. 50th ed. s.l.:WHO Food Additives.

Suranto, adji. 2004. Khasiat dan Manfaat Madu Herbal. Agro Media Pustaka. Jakarta

Teffer, K. & Semendeferi, K., 2012. Human prefrontal cortex: Evolution, development, and pathology. In: *Progress in Brain Research.* San Diego: Elsevier, pp. 191-218.

Teffer, K. & Semendeferi, K., 2012. Human prefrontal cortex: Evolution, development, and pathology. *Elsevier,* Volume 195.

Tortora, G. J. & Derrickson, B., 2011. *principles of anatomy & Physiology*.. 13 ed. New Jersea: John Wiley & Sons, Inc.

Wagh, V. G., 2013. Propolis: A Wonder bees product and its pharmacological potentials.. *Advances in Pharmacological Sciences.*.

Y. Gluhcheva, et al., 2012. Sodium nitrite-induced hematological and hemorheological changes in rats. *Series on Biomechanics*, Volume 27, pp. 53-58.

Biography

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