Mikania Micrantha Improved Memory Perform on Dementia Model

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Abstract

BACKGROUND: The purpose of this research is to explore the existing natural resources in Jambi province which has potential as anti-dementia agent. So that will be many natural resources that can be a potential product in reducing the unwanted effects of dementia as a degenerative disorder that is currently an inevitable elderly disease. by investigating with various plants in Jambi that have activities as anti-dementia is expected more and more natural resources that can be used as neuron-protection and or neuron-curative.

AIM: The purpose of this study is to find plants and / or compounds that are useful as neuroprotection

METHODS: Dementia model is formed by diabetic test animals. The test group consisted of extract group, three fractions (hexane, ethyl acetate and butanol fraction at dose 500 mg/Kg BB p.o) and one group of antidiabetic drugs glibenclamide, and the group of normal animal test animals was tested with Radial arm maze (RAM) for seven days before alloxan induced to obtain dementia model.

RESULTS: The results showed that extract and ethyl acetate fraction at dose 500 mg/Kg BW gave a positive effect on memory improvement based on animal performance on RAM tool during a testing time (P < 0.05) with LSD statistical analysis.

CONCLUSION: The extract and ethyl acetate fraction of Mikania micrantha showed good potential for improving the performance of animal memory in RAM devices representing dementia models.

Introduction

Dementia is a neurodegenerative disease that is linearly correlated with aging [1]. The incidence is reduced by age below 60 years. Dementia is characterized by a decrease in cognitive and behavioral function. Dementia is also a marker of progressive destruction of the brain's physiological function, Alzheimer's is one of the most frightening forms of dementia, hence numerous studies have been conducted both in vivo and in vitro to know more about the pathological path of dementia so that scientists can know how to prevent and treat the condition.

Recent studies have shown a link between the incidence of diabetes mellitus (DM) [2], [3], [4] and an increased risk factor for the occurrence of dementia. Dementia in diabetic patients is associated with an impairment of brain insulin receptors leading to a decrease in cognitive function (learning and remembering) and behavioral alterations presumably caused by cerebral inflammation [5], [6], [7].

Cucumber plant (Mikania micrantha K), which is a plant of the genus Asteracea, which until now only 42 species of plant families have been experiments on biological activity. Where the plant has anti-inflammatory, analgesic, anti-bacterial, anti-protozoa, antioxidant and cytotoxic. Recent research also mentions that mikania micrantha cultivation can be used for depression conditions. Therefore, in this study, we will conduct an investigation of anti-dementia activity test from mikania plant to animal model of diabetes mellitus which in induction alloxan.
Material and Methods

Material

Mikania micrantha, EtOH, Butanol, Ethyl Acetate, radial arm maze (RAM) [8] Gluco®®, rotary evaporator, analytic balance, alloxan, aquadest, glibenclamide.

Animal

The test animals used were white male mice of 2-3 months Mus musculus strain which was fed and drank well before testing of the test animal was fasted for 18 hours.

Methods

The dementia model was prepared by alloxan induction of 150 mg/kg i.p, in which all test animals showed a decreased cognitive ability to remember in the RAM test apparatus. During the acclimatization of the test animals, first use the cognition tool test using RAM [9], [8], [10]. The animal group was divided into 6 test groups, comprising Positive group (glibenclamide), Negative group (alloxan induction) 150 mg/Kg BW.

The extracted group and 3 fractions (ethyl acetate, butane, and hexane) dose 500 mg/kg p.o given for 28 days. And observations of blood glucose and cognitive changes in the tool RAM performed on days 7, 14, 21 and 28

Results

Observations during the test period showed a decrease in the blood glucose of test animals shown in Table 1.

Table 1: Glucose blood level

| Group | 1 | 7 | 14 | 21 | 28 |
|-------|---|---|----|----|----|
| Positive | 142.2 ± 5.5 | 103.8 ± 5.4 | 104.2 ± 5.2 | 115.8 ± 4.4 | 99 ± 4.6 |
| Negative | 338.8 ± 10.1 | 334.2 ± 12.7 | 270.8 ± 9.0 | 239.6 ± 10.3 | 240.2 ± 6.3 |
| Extract | 241.4 ± 4.7 | 200.2 ± 3.2 | 176.6 ± 2.7 | 137.9 ± 7.9 | 133.8 ± 5.7 |
| Ethyl acetate | 204 ± 3.6 | 185 ± 3.6 | 161 ± 2.9 | 141 ± 7.4 | 123.8 ± 3.6 |
| Butane | 250.2 ± 4.7 | 208 ± 6.7 | 179.8 ± 4.2 | 169 ± 4.0 | 160 ± 7.0 |
| Hexane | 276 ± 6.8 | 220 ± 3.4 | 204 ± 3.5 | 186 ± 4.7 | 171 ± 3.6 |

Table 2: Retention Time on RAM

| Group | 1 | 14 | 21 | 28 |
|-------|---|----|----|----|
| Positive | 297.2 ± 1.3 | 233.4 ± 1.7 | 198.1 ± 1.4 | 155 ± 1.6 |
| Negative | 600 ± 0 | 406.4 ± 2.3 | 420.8 ± 1.8 | 419 ± 0.9 |
| Extract | 288.2 ± 1.4 | 272.4 ± 1.8 | 217.8 ± 1.4 | 188.4 ± 1.3 |
| Ethyl acetate | 207.1 ± 1.3 | 176.6 ± 1.3 | 176 ± 1.3 | 176 ± 1.3 |
| Butane | 309.8 ± 1.3 | 265 ± 1.4 | 223.4 ± 1.6 | 203.4 ± 1.3 |
| Hexane | 316.4 ± 1.1 | 306.6 ± 2.9 | 290 ± 2.4 | 241.1 ± 2.9 |

Discussion

To see the impact of memory performance improvements on our RAM tools make animal models of dementia by using alloxan induction. in some previous journals have also mentioned that the rise in blood glucose, especially in diabetic patients believed to have a significant impact on the formation of dementia in correlation with cerebral vascular inflammation resulting in decreased cognitive abilities
and behavioral changes of diabetic patients. Cognitive decline, especially in the ability to learn and remember this is due to a decrease in sensitivity to insulin signals in the brain. Vascular inflammatory conditions and beta-amyloid plaque formation are believed to be closely related to the progress of the severity of Alzheimer's disease [2], [3], [11].

In this study showed that dementia animal model can be generated by alloxan induction, in which the increase of blood glucose in animal test resulted in the decrease of blood glucose level from all animal group of tests and decrease of blood glucose seen significantly in ethyl acetate group compared with group glibenclamide as a positive group. Compound compounds in plants that have anti-diabetic activity are believed to be from terpenoid group compounds that can reduce the damaging effects of excessive oxidation on pancreatic beta cells in this case as a result of alloxan induction. As a result of decreased oxidation reaction by this terpenoid, group compound showed improvement of blood glucose levels. The in vivo study of the Mikania micrantha plant showed that this plant had 13 identifiable sesquiterpen lactones compounds. Magnoliaceae are known to have excellent anti-inflammatoryary properties. Triterpenes and phytosterols are known to be widespread in plants from the Mikania family [12], [13], [14].

Improvements in memory performance in RAM assays showed significance in the ethyl acetate group of animals compared with the negative group and positive group by decreasing retention time and many faults from the test animals to find their food in the RAM device. When compared with the positive test animal group (glibenclamide), the ethyl acetate assay group gave significant improvement in memory performance in follow-up with the extract group. This reinforces the notion that the chemical compounds of the Mikania plant of the ethyl acetate fraction have activity against the memory improvement of the test animals. Because the dementia model derived from alloxan induction can reinforce the theory that diabetes is a risk factor of the incidence of dementia. Dementia as a pointer to the progressive destruction of nerve cells where the worst effects of dementia conditions are Alzheimer's disease that remains unaccounted for. However, the memory repair mechanism of the Mikania micrantha compound on memory improvement is still unclear, whether this memory repair works directly on the improvement of insulin signaling in the brain that will inhibit inflammation in the brain that can improve cognitive performance [2], [15], [13], [4] animal approach of this animal model of diabetes can be used as a preliminary study in studying the course of the disease from dementia. From the results obtained further research led the researcher to be able to continue to elude other dementia models to find a suitable mechanism to explain the pathological condition of dementia in order to lead to the discovery of compounds that can be used as neuro-protection and neuro-curative useful for further treatment [16], [17], [18], [8], [19].

In conclusion from the results of this study showed that Mikania micrantha has a positive activity on the central nervous system and can be used as an alternative plant as neuro-protection and neuro-curative.

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References

1. Gustafsson M, Karlsson S, Lövheim H. Inappropriate long-term use of antipsychotic drugs is common among people with dementia living in specialized care units. BMC Pharmacol Toxicol. 2013;14(1):10. https://doi.org/10.1186/2050-6511-14-10 PMid:23391323 PMCid:PMC3875309
2. Blázquez E, Velázquez E, Hurtado-Carneiro V, Ruíz-Albusac JM. Insulin in the brain: Its pathophysiological implications for states related with central insulin resistance, type 2 diabetes and Alzheimer’s disease. Front Endocrinol (Lausanne). 2014; 5:1-21. https://doi.org/10.3389/fendo.2014.00161 PMid:25346723 PMCid:PMC4191295
3. Stanley M, Macauley SL, Holtzman DM. Changes in insulin and insulin signaling in Alzheimer’s disease: cause or consequence? J Exp Med. 2016; 213(8):1375-85. https://doi.org/10.1084/jem.20160493 PMid:27432942 PMCid:PMC4986537
4. Takeda S, Sato N, Uchio-Yamada K, Sawada K, Kunieda T, Takeuchi D, et al. Diabetes-accelerated memory dysfunction via cerebrovascular inflammation and A deposition in an Alzheimer mouse model with diabetes. Proc Natl Acad Sci. 2010; 107(15):7036-41. https://doi.org/10.1073/pnas.1000645107 PMid:20231468 PMCid:PMC2872449
5. Balash Y, Mordechovich M, Shabati H, Giladi N, Gurevich T, Korczyn AD. Subjective memory complaints in elders: depression, anxiety, or cognitive decline? Acta Neurologica Scandinavica. 2013; 127(5):344–50. https://doi.org/10.1111/ane.12038 PMid:23215819
6. Buccafusco JJ. Methods of Behavior Analysis in Neuroscie, 2001. https://doi.org/10.1201/9781420041811
7. Deng W, Aimone JB, Gage FH. New neurons and new memories: How does adult hippocampal neurogenesis affect learning and memory? Nat Rev Neurosci. 2010; 11(5):339-50. https://doi.org/10.1038/nrn2822 PMid:20354534 PMCid:PMC2886712
8. Penley SC, Gaudet CM, Threlkeld SW. Use of an Eight-arm Radial Water Maze to Assess Working and Reference Memory Following Neonatal Brain Injury. 2013;(December):1-7. https://doi.org/10.3791/50940 PMid:24335781 PMCid:PMC4030456
9. Nair A, Jacob S. A simple practice guide for dose conversion between animals and humans. J Basic Clin Pharm. 2016; 7(2):27. https://doi.org/10.4103/0976-0166.177703 PMid:27057123
10. Kafle S, Shanbhag T, Shenoy S, Amuthan A, Prabhu K, Mohan S, Somayaji SN, Shrestha J. Antifertility effect of Areca catechu in male albino rats. Int J Pharm Sci Rev Res. 2011; 10(1):79-82.

11. Feng H, Dang H, Fan H, Chen X, Rao Y, Ren Y, et al. Curcumin ameliorates insulin signalling pathway in brain of Alzheimer's disease transgenic mice. Int J Immunopathol Pharmacol. 2016; 29(4):734-41. https://doi.org/10.1177/0394632016659494 PMid:27466310

12. Dong LM, Jia XC, Luo QW, Peng YM, Zhang Q, Luo B, et al. Four new ent-kaurene diterpene glucosides from Mikania micrantha. Phytochem Lett. 2017; 20:155-9. https://doi.org/10.1016/j.phytol.2017.04.029

13. Sodhi RK, Jaggi AS, Singh N. Animal models of dementia and cognitive dysfunction. Life Sciences. 2014; 109(2):73-86. https://doi.org/10.1016/j.lfs.2014.05.017 PMid:25066372

14. Xu Q, Xie H, Xiao H, Wei X. Phenolic constituents from the roots of Mikania micrantha and their allelopathic effects. Journal of agricultural and food chemistry. 2013; 61(30):7309-14. https://doi.org/10.1021/jf4017652 PMid:23822807

15. Jiwa NS, Garrard P, Hainsworth AH. Experimental models of vascular dementia and vascular cognitive impairment: A systematic review. J Neurochem. 2010; 115(4):814-28. https://doi.org/10.1111/j.1471-4159.2010.06958.x PMid:20731763

16. Bezzi P, Volterra A. Previews Astrocytes: Powering Memory. Cell. 2011; 144(5):644-5. https://doi.org/10.1016/j.cell.2011.02.027 PMid:21376229

17. Brodaty H, Donkin M. Family caregivers of people with dementia. Dialogues Clin Neurosci. 2009; 11(2):217-28.

18. Kuypers KPC, Theunissen EL, Wel JHP Van, Sousa EB De. Verbal Memory Impairment in Polydrug Ecstasy Users: A Clinical Perspective, 2016:1-16. https://doi.org/10.1371/journal.pone.0149438 PMid:26907605 PMCID:PMC4764468

19. Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W, Ferri CP. The global prevalence of dementia: A systematic review and metaanalysis. Alzheimer’s Dement. 2013; 9(1):63-75. https://doi.org/10.1016/j.jalz.2012.11.007 PMid:23305823