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# Development of Fruit and Vegetable Peels Extracts for Memory Improvement of Prevention and Treatment of Cognitive Impairment

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***Abstract***

*This study relates to a composition for improvement of memory or prevention and treatment of cognitive impairment using waste resources rich in beneficial substances. This study makes good effects to inhibit the activity of acetylcholinesterase in brain tissue and to improve the cognitive functions in a simulation model of cognitive impairment induced by scopolamine, so it can be available in the promotion of memory and the prevention and treatment of cognitive impairment. The composition uses the extract of fruit peels, which have long been used without causing toxicity in a wide range of food applications; therefore, it can be used safely without a risk of side effects, even in the case of a long-term administration for the preventive purpose. Furthermore, this research is a very beneficial invention in the environment-friendly aspect in association with the recycling of resources, as it is based on the novel efficacies of fruit peels, which have been conventionally disposed as a refuse of fruits due to their poor sensory qualities despite the content of beneficial substances.*

***Keywords:*** *Memory, Acetylcholinesterase, Scopolamine, Fruit and vegetable peels extract*

## 1. Introduction

Cognitive functions and memory are a major concern to the mass of modern people from teenagers to elderly people in a deluge of information increasing exponentially in the modern society. Impaired memory and cognitive problems preclude the possibility of social life as well as normal personal life and cause a high rise of social expenses. Especially, the impaired memory has a serious effect on the possibility of social life for those with dementia. In recent times, apart from the elderly people with senile dementia, a mass of young people are commonly suffering from so-called digital dementia, which means a deterioration of cognitive abilities concerning memory or calculation ability due to an overuse of digital technology, including mobile phones, PDAs, computers, or the like. The therapeutic agents for dementia currently available are galantamine, donepezil, and rivastigmine, which cause side effects, such as gastrointestinal problems, dizziness, headache, etc. Out of these agents, galantamine is an herb medicinal component extracted from a Bulgarian wildflower, snowdrop, and used as one of the representative therapeutic agents for dementia due to its cholinesterase inhibitory function. But, its safety is under reexamination in the FDA in the United States or the like, based on

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the two researches showing that the mortality rate is high in the patients taking a medication of galantamine[1, 2, 3, 4, 5]. Dementia is a general term that describes a wide range of symptoms associated with a decline in memory or other thinking skills, including mild memory loss, emotional disorder, personality disorder, behavior disorder, etc., severe enough to reduce a person's ability to perform everyday activities in the work, social life, and interpersonal relation. Alzheimer's disease accounts for an estimated 50 percent of dementia cases. It is known that the cognitive dysfunction in association with Alzheimer's disease results from the serious damage of parasympathetic nerves playing an important role in learning and memory activities and a decrease of the neurotransmitter, acetylcholine[6, 7].

The induction of cholinergic dysfunction is suggested as an effective simulation model for cognitive decline in human. Scopolamine, a drug having an antimuscarinic activity on the acetylcholine receptors in human body, increases the activities of acetylcholinesterase to break down acetylcholine and leads to a decline of cognitive abilities. It is therefore commonly used in the simulation models for the evaluation of new antidementia drugs. There are some studies on the use of cholinergic drugs, acetylcholine precursors, or acetylcholinesterase inhibitors for activating the cholinergic functions of brain to improve the cognitive abilities. On the other hand, fruit peels disposed as a refuse are rich in beneficial physiological components like minerals, vitamins, or polyphenols and thus expected to be available as an ingredient of new pharmaceutical or functional food compositions[8]. The development of products using fruit peels reduces a vast loss expense in the disposal of wastes and also possibly leads to a decrease in the factors of environmental contamination in the earth.

## 2. Experiment Materials

### 2.1 Preparation of fruit peel extract

Apples and pears, purchased from the Agricultural & Marine Products Market from March to June of 2018, were washed, removed of water, and peeled off. The fruit peels were dried out. The dried fruit peels were mixed with water in an internal container of a heat treatment device (Jisco, Jae Ile Co., Ltd., South Korea) tolerable under the pressure of 10 kg/cm$^2$, where the water as used herein was six times the volume of the dried fruit peels. The mixture sample was heated at 90 °C for 2 hours. The heat treatment device was designed to heat up the fruits in an external container at a predetermined temperature for a predetermined period of time in order to prevent the carbonization of the sample by a direct heat transmission. After the two-hour heating, the extract thus obtained was concentrated to a predetermined concentration, freeze-dried and then refrigerated [9].

## 3. Experiments Method

### 3.1 Evaluation of inhibitory activity against acetylcholinesterase in brain tissue

The single extracts of apple or pear peels and the composite extract of apple and peal peels (at mixing ratio of 1:1 (w/w)) prepared by the procedures of Example 1 were evaluated in regards to the inhibitory activity against acetylcholinesterase (AchE) in the brain tissue using an acetylcholinesterase (AchE) assay kit (Abcam, ab138871). In order to obtain a brain tissue from a mouse for the evaluation, an assay buffer was added to immerse a mouse brain tissue and the brain tissue was pulverized and centrifugally separated at 1,500 rpm for 5 minutes. Each fruit peel extract was added to the resultant supernatant containing the brain tissue to make a concentration of 5 to 500 μg/ml and treated at the room temperature for one hour. According to the manufacturer's instructions, the assay sample was treated with the reactant solution, protected from light to cause a reaction indoors for 30 minutes, and then measured in regards to the absorbance at 410 nm[10,11]. From the absorbance measurement, the AchE inhibition rate (%) was calculated according to the following equation:

AchE inhibition Rate (%) = [Absorbance of Sample/ Absorbance of Control] multiply 100

**3.2 Water maze test on mouse model with scopolamine-induced decline of learning and memory abilities.**

The 7-week old C57BL/6 mice were purchased from Daehan BioLink Laboratories (South Korea) and adapted to the lab environments for one week. Food (Samyang Co., Ltd., South Korea) and water were provided *ad libitum*, where the food was the standard diet composed of at least 22.1 % of crude protein, at most 8.0 % of crude fat, at most 5.0 % of crude fiber, at most 8.0 % of crude ash, at least 0.6 % of calcium, and at least 0.4 % of phosphorus. After the one-week adaptation, healthy mice were selected for the five-day repeated practices conducted once daily in a Morris water maze for one week. The Morris water maze used a water pool 90 cm in diameter and about 30 cm deep. The pool was filled to approximately two thirds of the 30cm depth with warm tap water, maintained at constant temperature of 27 °C. The escape platform was a cylinder 10 cm in diameter, placed in the center of the pool for the mice to scramble on. Mice were tested in one trial per day to select those that can scramble from the pool to the platform within 30 seconds. 10 selected mice were assigned to each group, that is, one control group and each sample group administered with a fruit peel extract (200 mg/kg). Then, the ten mice in each sample group were orally administered with an apple peel extract, a pear peel extract, or a composite extract of apple and pear peels once per day for one week and put into the repeated scrambling practices carried out three times a week [12]. In 30 minutes after the completion of the 14-day practices and 7-day drug administrations, the mice of each sample group were subjected to an intraperitoneal injection of scopolamine (1 mg/kg). In 30 minutes, each mouse was separately put into the Morris water maze and its behavior was examined using a video-tracking system. The behavior of the mouse was analyzed with a video-tracking software.

**3.3. Water maze test on mouse model with scopolamine-induced decline of learning and memory abilities.**

The 7-week old C57BL/6 mice were purchased from Daehan BioLink Laboratories (South Korea) and adapted to the lab environments for one week. Food (Samyang Co., Ltd., South Korea) and water were provided *ad libitum*, where the food was the standard diet composed of at least 22.1 % of crude protein, at most 8.0 % of crude fat, at most 5.0 % of crude fiber, at most 8.0 % of crude ash, at least 0.6 % of calcium, and at least 0.4 % of phosphorus.

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## 4. Result and Discussion

### 4.1 Evaluation of inhibitory activity against acetylcholinesterase in brain tissue

FIG. 1 showing the measurement results, the apple peel extract made no difference in the AchE inhibitory activity at varied concentrations, whereas the pear peel extract showed the AchE inhibitory activity dependent upon the concentration. The apple peel extract had the higher AchE inhibitory activity than the pear peel extract at relatively low concentrations of 5 to 50 μg/ml, but the pear peel extract had the far higher AchE inhibitory activity than the apple peel extract at concentrations of 100 μg/ml or above.

In particular, the composite extract of apple and pear peels was superior in the AchE inhibitory activity to the single extract of apple or pear peels. This explicitly showed the synergic effect resulting from the interactions of the ingredients by the combination and revealed the fact that the synergic effect increased with an increase in the concentration.

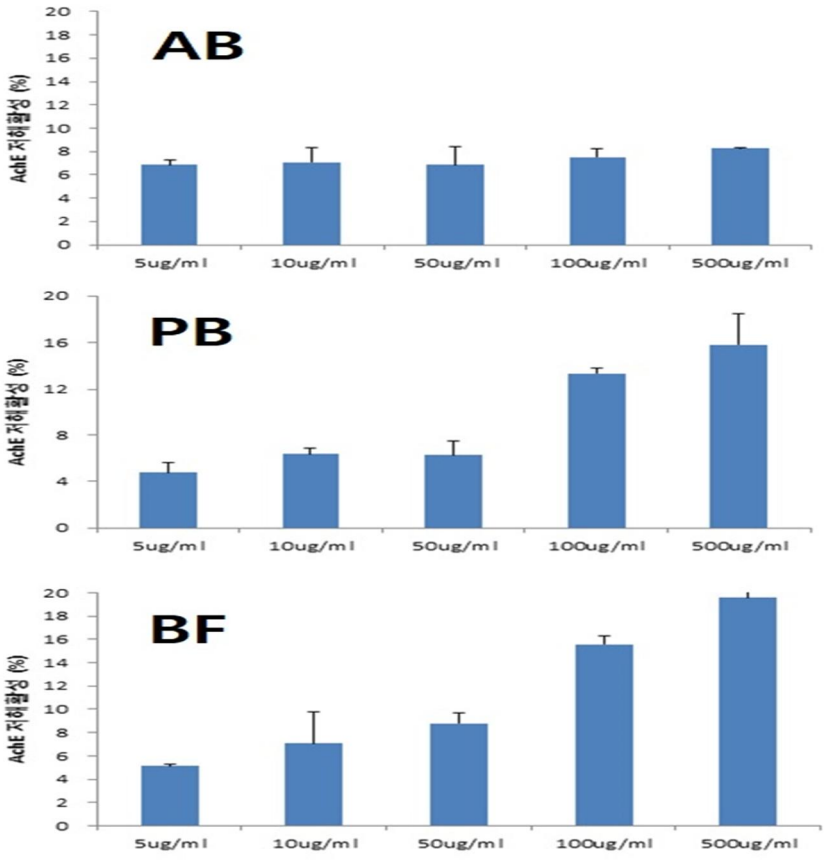


**Figure 1. The a graph showing the inhibitory activity of the novel composition against acetylcholinesterase.**

### 4.2 Water maze test on mouse model with scopolamine-induced decline of learning and memory abilities.

FIG. 2 shows the stop-through latency that is the required time for each mouse treated with scopolamine to arrive from the pool to the platform; and FIG. 3 shows the distance-through latency that is the quantity of motion made by each mouse at the pool while scrambling from the pool to the platform. As can be seen from FIGS. 2 and 3, the extract of apple or pear peels contributed to a great reduction of the latency induced by the

treatment with scopolamine, and the composite extract of apple and pear peels had a synergic effect in comparison to the single extract of apple or pear peels. The results of FIG. 2 and FIG.3 correspond to the result of FIG. 1.

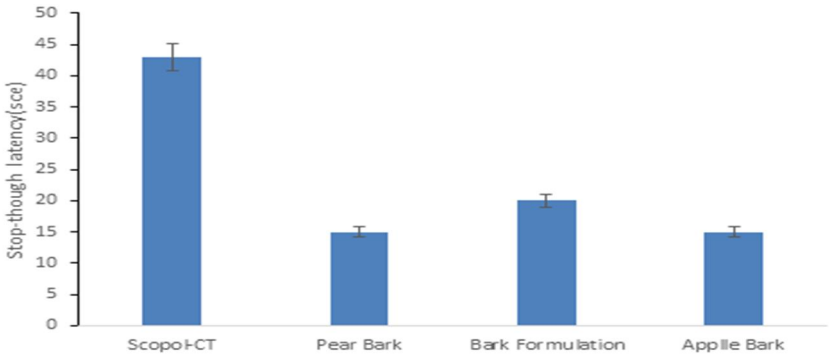


**Figure 2. The effects of the fruit peel extract on the stop-through latency in a water maze test.**

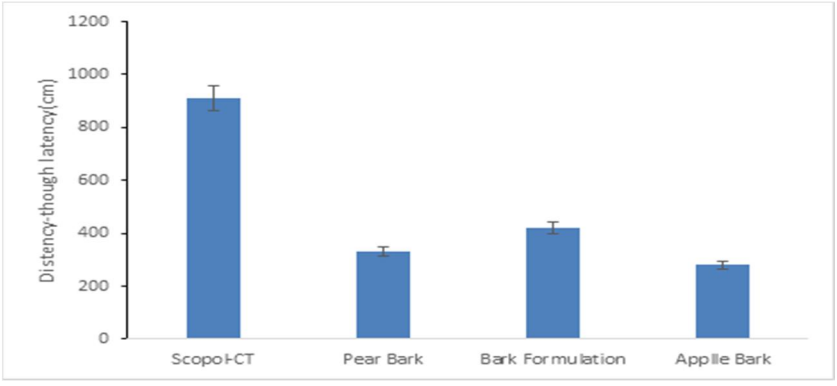


**Figure 3. The effects of the fruit peel extract on the distance-through latency in a water maze test.**

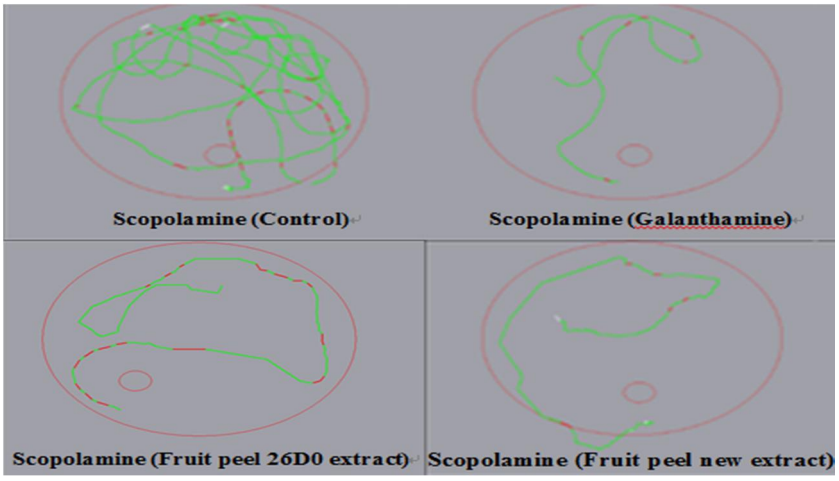


**Figure 4. The photograph on the memory deficit mice induced by scopolamine in the distance movement-through type Morris water maze test.**

## 5. Conclusion

The study relates to a composition for improvement of memory or prevention and treatment of cognitive impairment using waste resources rich in beneficial substances, and more particularly to a composition for improvement of memory or prevention and treatment of cognitive impairment that includes an extract of apple or pear peels. It is therefore an object of the present invention to provide a novel composition for improvement of memory or prevention and treatment of cognitive impairment that can be used with safety by studying the physiological activities of a resource conventionally used as a food resource for a long time to guarantee its safety to the human body, but not studied sufficiently in regards to its benefits due to poor sensory qualities and hence disposed as a refuse. For achieving the object of the present research is directed to a pharmaceutical composition for improvement of memory or prevention and treatment of cognitive impairment that includes an extract of apple or pear peels. As described above, this research makes good effects to inhibit the activity of acetylcholinesterase in brain tissue and to improve the cognitive functions in a simulation model of cognitive impairment induced by scopolamine, so it can be available in the promotion of memory and the prevention and treatment of cognitive impairment.

The composition of the fruit peel extract uses the extract of fruit peels, which have long been used without causing toxicity in a wide range of food applications; therefore, it can be used safely without a risk of side effects, even in the case of a long-term administration for the preventive purpose. Furthermore, the fruit peel extract is a very beneficial substances in the environment-friendly aspect in association with the recycling of resources, as it is based on the novel efficacies of fruit peels, which have been conventionally disposed as a refuse of fruits due to their poor sensory qualities despite the content of beneficial substances.

## References

[1] S. C. Kim, “A Low-Complexity antenna selection algorithm for quadrature spatial modulation systems,” *International Journal of Internet, Broadcasting and Communication (IJIBC)*, Vol.9, No.1, pp.72-80, January 2017 DOI: https://doi.org/10.7236/IJIBC.2017.9.1.72.

[2] J. S. Jung, J. Kwon, S. H. Jung, M. W. Lee, V. Mariappan, and J. S. Cha, “Impact of SV40 T antigen on two multiple fission microalgae species Scenedesmus quadricauda and chlorella vulgaris,” *International Journal of Advanced Smart Convergence(IJASC)*, Vol.6, No.1, pp.82-88, March 2017. DOI: https://doi.org/10.7236/IJASC.2017.6.1.82.

[3] E. G. Ahmed, and H. Y. Seung, “ Impact of SV40 T antigen on two multiple fission microalgae species scenedesmus quadricauda and chlorella vulgaris,” *International Journal of advanced smart convergence(IJASC)*, Vol. 7, No. 1, pp. 48-63, June 2018. DOI: http://dx.doi.org/10.7236/IJASC.2018.7.1.7.

[4] H. J. Jeon, J. Hafeez, A. Hamacher, S. Lee, and S. C. Kwon, “ A study on the quality of photometric scanning under variable illumination conditions,” *International Journal of advanced smart convergence(IJASC)*, Vol. 6, No. 4, pp. 88-95, June 2017. DOI: http://dx.doi.org/10.7236/IJASC.2017.6.4.13.

[5] A. Nordberg, “Pharmacological treatment of congnitive dysfunction indementia disorders”, *Acta. Neurol. Scand. Suppl.*, Vol. 168, pp. 87-92, December 1996. DOI: http://doi.org/10.1111/j.1600-0404.1996.tb00379.x.

[6] M. G. Giovannini, F. Casamenti, L. Bartolini, and G. Pepeu, “The brain cholinergic system as atarget of cognition enhancers”, *Behaviour Brain Research*, Vol. 83(1-2), pp. 1-5, February1997. DOI: http://doi.org/10.1016/S0166-4328(97)86038-X.

[7] V. Fodale, D. Quartrone, C. Trecroci, V. Caminiti, and LB. Scantamaria, "Alzeheimer's disease and anaesthesia: implications for the central cholinergic system", *Br. J. Anaesth*., Vol. 97(4), pp. 445-452, September 2006. DOI: http://doi.org/10.1093/bja/ae1233.

[8] RT. Bartus, "On neurodegenerative disease, model and treatment strategies: lessons learned and lessons forgotten a generation following the cholinergic hypothesis", *Exp. Neurol*., Vol. 163(2), pp. 495-529, June 2000. DOI: http://doi.org/10.1016/exnr.2000.7397.

[9] K. Mishima, K. Iwasaki, H. Tsukikawa, Y. Matsumoto, N. Egashira, and K. Abe, "The Scopolamine-induced impairment of spatial cognition parallels the acetylcholine release in the ventral hippocampus in rats", *Jpn. J. Pharmacol*., Vol. 84(2), pp. 163-173, October 2000. DOI: http://doi.org/10.1254/jjp.84.163.

[10] N.Yamada, A.Hattori, T. Hayashi, T. Nishikawa, H. Fukuda, and T. Fujino, "Improvement of scopolamine-induced memory impairment by Z-ajoene in the water maze in ice", *Pharmacol. Biochem, Behav*., Vol. 78(4), pp. 787-791, August 2004. DOI: http://doi.org/10.1016/j.pbb.2004.05.017.

[11] R. Khonkarn, S. Okonogi, C. Ampasavate, and S. Anuchapreeda, "Investigation of fruit peel extacts as sources for compounds with antioxidant and antiproliferative activities against human cell lines", *Food. Chem. Toxicol*., Vol. 48(8-9), pp. 2122-2129, August-Sepember 2010. DOI: http://doi.org/10.1016/j.fct.2010.05.014.

[12] P. Davies, and AJ. Maloney, "Selective loss of central cholinergic neuros in Alzheimer type disease", *Lancet*., Vol. 25(2), pp. 1403-1408, December 1976. DOI: http://doi.org/10.1016/S0140-6736(76)91936-X.

[13] H. R, Maei, K. Zaslavsky, A. H. Wang, A. P. Yiu, C.M. Teixeira, S. A. Josselyn, and P. W. Frankland, "Development and validation of a sensitive entropy-based measure for the water maze", *Front Integr Neurosci.* , Vol. 4(3), pp. 33-40, December 2009. DOI: http://doi.org/10.3389/neuro.07.033.2009.

[14] S. Hestrin, "The reaction of acetylcholine and other carboxylic acid derivatives with hydroxylamine, and its analytical application", *Journal of Biological chemistry*., Vol. 180(1), pp. 249-261, August1949.