Plant Nutrition & Soil Science International (2024)
Clausius Scientific Press, Canada

DOI: 10.23977/pnssi.2024.030102
ISSN 2616-1745 Vol. 3 Num. 1

Experimental Study on the Effects of Guangxi Sweet Tea and Shutangbao on β-amyloid Protease 1 (BACE1) and Cognitive and Memory Functions in Mice Exposed to Maltol Aluminum

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Keywords: Mice; Blood Sugar; Learning and Memory Ability; Aluminum Maltol; BACE1; Treatment

Abstract: To explore the impacts of Guangxi sweet tea and Shutangbao on β-amyloid protease 1 (BACE1) in aluminum maltol-poisoned mice and compare their effects on mice's cognitive and memory functions. Sixty KM mice were randomly grouped. Mice in the model group, treatment group 1 (with Guangxi sweet tea), and treatment group 2 (with Shutangbao) were intraperitoneally injected with 0.3ml aluminum maltol solution per mouse for 30 days. The Y-maze test measured memory[1]. Serum and brain tissue were sampled for relevant detections including biochemical indicators and enzyme activities. For blood glucose, significant differences were seen among groups before and after modeling and after taking medicine. For enzyme activities, β-secretase increased in the model group but decreased in treatment groups. α- and γ-secretase activities were higher in the normal group. These enzyme changes are closely related to the pathological process of Alzheimer's disease, suggesting that the intervention of sweet tea and Shutangbao may have a positive impact on alleviating cognitive impairment. Both sweet tea and Shutangbao can lower blood glucose. Aluminum maltol affects BACE1 expression, impairing memory. They may regulate BACE1 via blood glucose reduction and improve memory effectively.

1. Preface

Alzheimer's Disease (AD), a progressive neurodegenerative disease, its main pathological features include the deposition of β-amyloid protein (Aβ) to form senile plaques and neurofibrillary tangles,

leading to neuronal damage and cognitive impairment [2]. In recent years, studies have revealed the potential toxic effects of aluminum in the nervous system, especially its influence on the expression of β-site amyloid precursor protein cleaving enzyme 1 (BACE1). Previous studies have found that the expression level of BACE1 in the frontal cortex with Aβ deposition is three times that of the cerebellum without Aβ deposition, suggesting that BACE1 plays an important role in the generation process of Aβ[3]. Existing studies have pointed out that aluminum can inhibit the activity of key enzymes in neurons. Al3+ has an inhibitory effect on the activities of ATPase, superoxide dismutase (SOD), and calcium-modulated erythrocyte membrane Ca2+-Mg2+-ATPase, and has a strong affinity with DNA in the neurofibrillary tangles, which is an important mechanism of aluminum poisoning[4]. Abnormal blood sugar levels, as the main characteristic of diabetes, are also closely related to an increased risk of developing AD. The hyperglycemic state not only directly damages neurons but also may indirectly promote the generation of Aβ by up-regulating the expression of BACE1, forming a vicious cycle and accelerating the pathological process of AD. In this context, Guangxi sweet tea and Shutangbao, as traditional herbs, have shown potential in blood sugar control [5][1]. Preliminary studies have shown that these natural plant extracts may reduce the accumulation of Aβ by inhibiting the abnormal expression of BACE1 through lowering blood sugar levels, providing a new path for the treatment of AD.

This study aims to prepare an aging model by intraperitoneal injection of aluminum maltol in mice, and explore the effects of Guangxi sweet tea and Shutangbao on β-amyloid protease 1 (BACE1) production in mice poisoned by aluminum maltol and compare the cognitive and memory functions of mice. By exploring the effects of aluminum maltol poisoning on the neurological function of mice, further clarify the mechanisms of Guangxi sweet tea and Shutangbao in regulating blood sugar, inhibiting BACE1 activity, and improving cognitive function.

2. Materials and methods

2.1. Materials

2.1.1. Experimental animals

Sixty healthy standard clean-grade mice were provided by Changsha Tianqin Biotechnology Co., Ltd. with license number Scxk (Xiang) 2019-0013. Half of them are male and half are female. They are 8 weeks old and weigh about 30g with similar activity ability. After being fed in the animal room for one week, they are caged according to body weight and gender, with five mice in each cage.

2.1.2. Reagents and drugs

Aluminum chloride, maltol, sodium chloride, 95% ethanol, normal saline, sweet tea, Shutangbao, o-toluidine, thiourea, boric acid, glacial acetic acid, acetylcholinesterase (AchE) test kit, triglyceride (TG) test kit, protein test kit (biuret method), total cholesterol (TC) test kit, protein test kit (Coomassie brilliant blue method), urea nitrogen test kit (urease method), glucose test kit (oxidase method), β-secretase (β-Secretase) test kit, α-secretase (α-Secretase) test kit, γ-secretase (γ-Secretase) test kit, etc.

2.1.3. Main instruments

Microplate reader, spectrophotometer, high-precision pipette and tips, constant temperature water bath, centrifuge, refrigerator, etc.

2.2. Methods

2.2.1. Experimental method

The mice were divided into normal control group, model group, treatment group 1 and treatment group 2, with 15 mice in each group. The model group, treatment group 1 and treatment group 2 were poisoned: maltol aluminum solution was made by mixing equal volumes of maltol solution and aluminum trichloride solution, and 0.3ml/mouse was intraperitoneally injected once a day for 6 consecutive days with a one-day interval for a total of 30 days. Then, streptozotocin solution was intraperitoneally injected into mice at a dose of 50-55mg/kg for 5 consecutive days once a day. The blood sugar of all mice before modeling was measured. After 72 hours, the blood sugar was measured. Mice with "three more" symptoms and blood sugar greater than 11.0mmol/L were selected as the aging diabetes model. After the blood sugar stably increased, the modeled mice were divided into three groups: untreated model group, intraperitoneal injection of maltol aluminum 0.45ml/mouse for 15 days; sweet tea treatment group, intragastric administration of sweet tea 0.3ml/mouse for treatment for 15 days; Shutangbao treatment group, intragastric administration of Shutangbao 0.3ml/mouse for treatment for 15 days.

2.2.2. Mouse learning and memory ability test and Y-shaped water maze experiment

The construction of the Y-shaped water maze model and the specific experimental method refer to the literature. The purpose is to test the memory function of mice through this experiment. Ten days before establishing the aluminum poisoning model in mice, the mice were trained on the memory of the water maze. Each mouse was trained three times a day. Then, it was measured continuously for three days. The landing time, error times and failure times of the mice were recorded. The overtime rate, error rate and failure rate of the mice were calculated. If the mouse fails to land correctly within 10 seconds, it is overtime. If the mouse swims in the wrong direction, it is an error. If the mouse fails to land correctly within 40 seconds, it is a failure. The tests were conducted in the early, middle and late stages before and after establishing the aluminum poisoning model in mice. Each stage was tested continuously for three days. Each mouse was tested three times a day. The test data were recorded[6].

2.2.3. Blood sugar determination (o-toluidine trace method)

Take 20μl of mouse tail blood and add it to an EP tube containing 0.2ml of saturated boric acid solution. Then add 30% trichloroacetic acid, mix well, centrifuge at 5000rpm for 5 minutes, and take the supernatant.

2.2.4. Determination of various biochemical indexes of mouse serum

Tc is determined by COD-CE-PAP; TG is determined by GPO-OAO method; urea nitrogen is determined by urease wave method; AchE is based on the fact that acetylcholine generates acetic acid and choline under the catalysis of AchE. Choline then reacts with a sulfhydryl chromogenic agent to produce a yellow compound TNB (symmetrical trinitrobenzene), and colorimetric determination is performed. The specific operation is in accordance with the kit instructions.

2.2.5. Preparation of 10% brain homogenate of mice and determination of secretase

The mice were sacrificed by cervic`al dislocation. The brain tissue was taken, the surface blood was washed off with 0.01M, PH7.4 phosphate buffer solution, and then the excess water was gently absorbed with filter paper. After weighing on a balance (g), the brain was placed in a glass homogenizer. Appropriate amount of phosphate buffer (0.01M, PH=7.4) was added. The grinding

was performed for 10 minutes under ice bath to prepare 10% brain homogenate. The activities of β-secretase (β-Secretase), α-secretase (α-Secretase) and γ-secretase (γ-Secretase) in mouse brain homogenate were determined by double antibody sandwich method (ELISA detection method). The detailed operation is in accordance with the instructions.

2.2.6. Statistical processing spss13 software

Analysis of variance was performed on the detection data. The results are expressed as (±s). The data between groups were compared with each other. If the analysis result is $P<0.05$ or $P<0.01$, the difference is statistically significant. The results were processed and analyzed by SPSS13.0 statistical software. The data are expressed as (±S), and analysis of variance and Q test were performed.

3. Results

3.1. Survival status of mice in each group

In the normal group of 15 mice, no mice died. In the model group of 15 mice, one died. In the treatment group 1 of 15 mice, two died. In the treatment group 2, no mice died.

3.2. Comparison of relevant data of mice in each group shows

3.2.1. Results of the determination of the activities of brain β-secretase, α-secretase, and γ-secretase (u/L) in mice

The results showed that the activity of brain β-secretase increased in the model group and decreased in the treatment groups; the activity of brain α-secretase in the normal group was higher than that in other groups, and the activity of brain γ-secretase in the normal group was higher than that in other groups. See Tables 1, 2, 3, and 4.

Table 1: Comparison of brain β-secretase, α-secretase, and γ-secretase (u/L) in mice of each group (±S)

group	Brain β-secretase 1.	Brain α-secretase.	Brain γ-secretase.
normal group	12.87±1.77▲★	10.39±2.00▲	16.60±3.27
model group	13.19±1.07▲▲★★	10.07±2.42▲	15.50±1.55
treatment group 1	11.64±1.09	9.49±2.50	15.70±1.16
treatment group 2	11.85±0.86	8.08±1.38	15.83±0.68

Analysis of variance: Comparison between groups: For brain β-secretase: $F = 5.163$, $P = 0.003$. Compared with treatment group 1, ▲$P < 0.05$, ▲▲$P < 0.01$, the difference is statistically significant. Compared with treatment group 2, ★$P < 0.05$, ★★$P < 0.01$, the difference is statistically significant. For brain α-secretase: $F = 2.958$, $P = 0.041$. Compared with treatment group 2, ▲$P < 0.05$, the difference is statistically significant. For γ-secretase: $F = 0.908$, $P = 0.443$, there is no statistically significant difference.

3.2.2. Comparison of water maze test time (s) of mice in each group before, during and after poisoning.

Analysis of variance: Comparison between groups: Before poisoning, comparison among groups showed $F = 1.297$, $P = 0.286$, $P > 0.05$, with no statistically significant difference; during poisoning (s), $F = 8.998$, $P = 0.000$. Compared with the normal group, ▲▲ < 0.01, with statistically

significant difference; after poisoning (s), F = 27.483, P = 0.000. Compared with the model group, ▲▲ < 0.01, with statistically significant difference. Comparison within groups in the early, middle and late stages: Normal group: F = 0.070, P = 0.933, P > 0.05. Comparison among the early, middle and late stages showed no statistically significant difference; Model group: F = 5.771, P = 0.006. Compared with before poisoning: a < 0.01, with statistically significant difference; Treatment group 1: F = 9.765, P = 0.000. Compared with during poisoning: b < 0.01, with statistically significant difference; Treatment group 2: F = 8.136, P = 0.001. Compared with during poisoning: c < 0.01, with statistically significant difference.

Table 2: Comparison of water maze test time (s) of mice in each group before, during and after poisoning (±S)

group	number of animals	Before poisoning (s).	During poisoning (s).	After poisoning (s).
normal group	13	3.59±0.39	3.66±0.55	3.65±0.46▲▲
model group	13	3.89±0.51	4.76±0.83▲▲	5.43±0.81a
treatment group 1	13	3.48±0.81b	5.14±1.03▲▲	3.61±0.65▲▲b
treatment group 2	13	3.77±0.41c	4.57±0.47▲▲	3.66±0.46▲▲c

3.2.3. Comparison of blood sugar after taking medicine in each group (±S)

Table 3: Comparison of blood sugar before and after taking medicine in mice of each group (±S) (mmol/L)

group	number of animals	Before taking medicine	After taking medicine, it ends
normal group	15	5.89±1.98★★	5.57±0.90
model group	15	11.93±4.45▲▲	7.36±0.74▲▲
treatment group 1	15	9.28±3.31▲▲★	7.48±0.15▲▲
treatment group 2	15	10.28±1.61▲▲	7.18±0.30▲▲

Analysis of variance: Comparison between groups: After taking medicine, comparison among groups showed F = 9.915, P = 0.000. Compared with the normal group, ▲P < 0.05, ▲▲P < 0.01, the difference is statistically significant. Compared with the model group, ★P < 0.05, ★★P < 0.01, the difference is statistically significant. At the end of taking medicine, F = 28.551, P = 0.000. Compared with the normal group, ▲▲P < 0.01, the difference is statistically significant.

3.2.4. Comparison of body weight of mice in each group, comparison within groups

Analysis of variance: Comparison between groups: In the early stage, comparison among groups showed F = 1.808, P = 0.156. Compared with the normal group, ▲P < 0.05, and the difference is statistically significant. In the middle stage: comparison among groups showed F = 7.601, P = 0.000. Compared with the normal group, ▲▲P < 0.01, and the difference is statistically significant. At the end of the later stage, comparison among groups showed F = 10.724, P = 0.000. Compared with the normal group, ▲P < 0.05, ▲▲P < 0.01. Compared with treatment group 1, ★P < 0.05, ★★P < 0.01, and the difference is statistically significant. Comparison within groups: Comparison among the early, middle and late stages: In the normal group, F = 71.207, P = 0.000. Compared with the early stage, a < 0.01. Compared with the middle stage, b < 0.01. The body weight continuously increases, and the difference is statistically significant. In the model group, F = 12.994, P = 0.000. Compared with the early stage, a < 0.01, and the difference is statistically significant. The increase from the early stage to the middle stage is obvious, while the increase from the middle stage to the

later stage is not obvious. In treatment group 1, F = 2.720, P = 0.078. Compared with the early stage, c < 0.05, and the difference is statistically significant. The increase from the early stage to the middle stage is not obvious, and there is a certain increase from the middle stage to the later stage. In treatment group 2, F = 16.590, P = 0.000. Compared with the early stage, a < 0.01, and the increase in both the early and middle stages is obvious.

Table 4: Comparison of body weight of mice in each group (±S) (g)

group	number of animals	Early stage of experiment.	mid-term	later stage
normal group	15	32.11±1.60^{b}	44.37±4.00^{a}	47.35±4.31★★^{ab}
model group	15	32.10±1.21	36.42±4.74▲▲^{a}	40.77±6.26▲▲★^{a}
treatment group 1	15	31.82±1.54	34.67±4.88▲▲	35.01±5.67▲▲^{c}
treatment group 2	15	31.03±1.49▲	37.97±5.91 ▲▲^{a}	41.69±6.93▲★★^{a}

3.2.5. Results of the determination of mouse brain AchE, serum urea nitrogen, and total protein

The results showed that there was no statistically significant difference in the comparison of AchE between groups. In the comparison of serum urea nitrogen between groups, there is a statistically significant difference. For total protein: there is no statistically significant difference. See Table 5.

Table 5: Comparison of mouse brain AchE, serum urea nitrogen, and total protein in each group (±S)

group	number of animals	AchE	urea nitrogen	Total protein (TP).
normal group	15	0.09±0.02	9.82±3.97	70.90±6.85
model group	15	0.09±0.02	7.98±1.91▲	71.23±5.80
treatment group 1	15	0.10±0.02	7.20±0.97▲▲	69.70±6.78
treatment group 2	15	0.08±0.02	8.39±2.54 ▲▲^{a}	69.34±7.25

Analysis of variance: Comparison between groups: For brain AchE, F = 1.222, P = 0.311, with no statistically significant difference; for serum urea nitrogen, F = 2.988, P = 0.039. Compared with the normal group, ▲P < 0.05, ▲▲P < 0.01, with statistically significant difference; for serum total protein: F = 0.264, P = 0.851, with no statistically significant difference.

3.2.6. Results of the determination of serum total cholesterol (TC) and triglyceride (TG) in mice of each group

The results showed that in the comparison of serum TC between groups, there is a statistically significant difference. In the comparison of serum TG between groups, there is a statistically significant difference. See Tables 6 for details.

Analysis of variance: Comparison between groups: For serum total cholesterol (TC): F = 11.820, P = 0.000. Compared with the normal group, ▲▲P < 0.01, and the difference is statistically significant. For serum TG: F = 26.315, P = 0.000. Compared with treatment group 2, ▲▲P < 0.01, and the difference is statistically significant; compared with treatment group 1, ★★P < 0.01, and the difference is statistically significant.

Table 6: Comparison of serum TC and TG in mice of each group (±S)

group	number of animals	TC (mmol/L)	TG(mmol/L)
normal group	15	5.92±3.32	2.86±1.02▲▲★★
model group	14	3.45±0.96▲▲	2.57±0.51▲▲★★
treatment group 1	13	2.77±0.86▲▲	1.25±0.55▲▲
treatment group 2	15	2.22±0.47▲▲	4.60±1.54★★

4. Discussion

4.1. The characteristic of diabetes is hyperglycemia

This phenomenon is due to the dysfunction of pancreatic lymphoid B cells and the subsequent reduction in systemic insulin sensitivity. Diabetes is mainly divided into two types [7]: type 1 diabetes and type 2 diabetes. 1. Type 1 diabetes, also known as insulin-dependent diabetes, often occurs in children and adolescents. Its pathogenesis is mainly due to the islet β cells being damaged by autoimmune attacks or other unknown reasons, resulting in an absolute deficiency of insulin secretion. Insulin is a key hormone for regulating blood sugar. It can promote cells to take up glucose and convert it into energy or store it. Once the secretion of insulin is in a state of severe deficiency, blood sugar is difficult to enter cells effectively, and then the blood sugar level rises. Type 2 diabetes is the most common type and accounts for the majority of diabetic patients. Its pathogenesis is more complex and is the result of the combined action of multiple factors. In terms of experimental results, after the modeling is completed, the blood sugar levels of each group are significantly higher than before modeling. However, before modeling, the blood sugar differences between groups are not statistically significant. After modeling is completed, the differences between the modeling groups are also not significant. After comparing each group after taking medication for treatment, the blood sugar of the model group is significantly higher than that of treatment group 1, treatment group 2 and the normal group. This shows that the blood sugar of the treatment group is significantly reduced after treatment, and the normal group is slightly higher than before treatment[8]. After taking medication for treatment in the modeling group, although the overall blood sugar increase level shows a significant difference compared with before modeling, the difference amplitude is not very high. The cause of this situation may be related to factors such as the low dosage of modeling reagents, the older age of mice, the higher body weight or the breed of mice. It needs to be discussed[8].

4.2. The drug used in treatment group 1 is Guangxi sweet tea, and the drug used in treatment group 2 is Shutangbao oral liquid

The treatment doses of the two are the same. Judging from the treatment effect, the blood sugar reduction amplitude of treatment group 1 is greater than that of treatment group 2, indicating that Guangxi sweet tea has better blood sugar-lowering ability. When comparing the blood sugar levels after modeling and after treatment, we observed that the blood sugar of the model group did show a certain degree of decline. However, compared with the specialized treatment group, the decrease in blood sugar in the model group is relatively mild, suggesting that the intervention measures of the treatment group may show more significant efficacy in regulating blood sugar. This shows that specific treatment methods can more effectively promote the normalization of blood sugar levels. Compared with the model group, its advantages in blood sugar control are more prominent. This difference may be attributed to the strategies or drugs used in the treatment group. They may have stronger efficacy or higher specificity in reducing blood sugar, thus achieving better treatment

effects. After treatment, comparison of each group shows that the treatment group is significantly lower than the model group, reflecting the curative effects of both Guangxi sweet tea and Shutangbao in reducing blood sugar. Comparing the normal group before modeling, after modeling and after treatment, although the blood sugar is within the normal range, it is significantly lower after modeling than before modeling and after treatment. This may be related to factors such as the degree of fasting of mice, blood collection time, and standard glucose during measurement. It needs to be studied[8].

4.3. Most studies believe that the excessive production and accumulation of β-amyloid protein (β-amyloidprotein, Aβ) may be the common pathway for various causes to induce AD [9]

Excessive aluminum has many harms in the human body. The most common harm is that aluminum may damage the nervous system, affect the normal function of the brain, lead to symptoms such as memory loss, decreased intelligence, and sluggish response, and even increase the risk of Alzheimer's disease. AI3+, that is, trivalent aluminum ion, shows a significant inhibitory effect on the function of key biomolecules. Its targets include the ATPase enzyme system, superoxide dismutase (SOD), and the Ca2+-Mg2+-ATPase of erythrocyte membranes activated by calmodulin. This series of inhibitory effects not only reveals the potential interference mechanism of trivalent aluminum ions on energy metabolism and antioxidant defense systems at the cellular level, but also implies its central role in the pathogenesis of neurodegenerative diseases. It is particularly worth noting that the high affinity of trivalent aluminum ions for DNA inside neuronal microfibril tangles is considered to be a crucial link in the pathological process of aluminum poisoning. This affinity may lead to abnormal changes in DNA structure through direct or indirect pathways, thereby affecting gene expression and protein synthesis, and finally contributing to neuronal dysfunction and apoptosis, becoming one of the key mechanisms for neurodegenerative diseases caused by aluminum poisoning. This discovery not only deepens our understanding of the mechanism of aluminum ion toxicity, but also provides an important theoretical basis for the development of effective prevention and treatment strategies for aluminum poisoning. In addition, acetylcholinesterase in the brain has a significant impact on the memory function of the mouse brain. The main function of AchE is to hydrolyze the neurotransmitter acetylcholine (ACh). When the content of AchE in the brain is too high, it will quickly decompose ACh, resulting in a decrease in the level of ACh. And ACh plays a key role in the learning and memory process. Insufficient content will affect nerve signal transmission, and then the content of (AchE) impairs the memory formation and consolidation ability of mice, showing symptoms such as memory impairment and decreased learning ability. On the contrary, if the content of AchE in the brain is reduced and the decomposition of ACh is reduced, its content in the brain will relatively increase, which will help enhance nerve signal transmission and may improve the memory function of mice. Judging from the results of this experimental study, comparison between groups: brain AchE, $F = 1.222$, $P = 0.311$ ($P > 0.05$), there is no statistically significant difference; indicating that the decline in memory function of mice in this experiment is not affected by the content of (AchE). The Y-shaped water maze test method is a recognized behavioral system that can better detect the spatial learning and memory ability of animals. The changes in swimming distance status, required time and number of mistakes can intuitively reflect the spatial positioning learning ability of experimental animals [10]. Judging from this experimental study, intraperitoneal injection of aluminum maltol can significantly prolong the time and swimming distance required for mice to explore the Y-shaped water maze, indicating that intraperitoneal injection of aluminum maltol will seriously damage the spatial memory and learning ability of mice. However, after poisoning, compared with the model group in treatment groups 1 and 2 and the normal group, $P < 0.05$, the difference is

statistically significant; there is a statistically significant difference in the comparison before, during and after poisoning in treatment group 1 and treatment group 2, indicating that Guangxi sweet tea and Shutangbao may be effective in improving the memory function of mice.

β-site APP cleaving enzyme 1 (BACE1, β-secretase) is a type I transmembrane aspartic protease composed of 501 amino acids and is mainly expressed in neurons in the brain. Previous scientific research has revealed a remarkable discovery: in the frontal cortex region where there is deposition of β-amyloid protein (Aβ), the transcription level of β-secretase 1 (BACE1) is significantly increased, and its expression abundance is three times higher than that of cerebellar tissue not affected by Aβ. This observation deeply suggests that BACE1 plays an indispensable central role in the Aβ generation pathway. The up-regulation of its activity may directly promote the production and accumulation of Aβ peptides, thereby posing a threat to the normal physiological functions of neurons and becoming a key link in the pathogenesis of neurodegenerative diseases such as Alzheimer's disease. BACE1, that is, β-site APP cleaving enzyme 1, is an aspartic protease. Its main role is to participate in the processing of amyloid precursor protein (APP) as β-secretase. Specifically, the cleavage of APP by BACE1 will lead to the production of two fragments, namely the soluble APPβ fragment and the membrane-bound C-terminal fragment (C99). C99 will then be further processed by γ-secretase to generate β-amyloid proteins such as Aβ40 and Aβ42[11]. Aβ42 is highly neurotoxic and can aggregate to form "senile plaques", which is one of the neuropathological features of Alzheimer's disease. In the brain tissues of patients with sporadic Alzheimer's disease, the expression and activity of BACE1 usually increase. In this experiment, an animal model of nervous system damage was prepared by intraperitoneal injection of aluminum maltol to poison mice. It was detected that aluminum exposure can cause an increase in the expression level of BACE1 in the mouse brain, and progressively simulate the conditions for the decline of related learning and memory abilities step by step in mice due to aluminum poisoning. It was found that when β-site APP cleaving enzyme 1 (BACE1) increases, α-secretase gradually decreases. This will cause the production of a greater amount of β-amyloid protein Aβ. The accumulated Aβ can inhibit the growth of nerve cells, tangle proteins and destroy the communication between brain cells through direct or indirect neurotoxic effects, and finally lead to direct cell death, thereby affecting learning and memory abilities and cognitive dysfunction. The difference in β-secretase between mice treated with Guangxi sweet tea and Shutangbao respectively and the model group is statistically significant, proving that Guangxi sweet tea and Shutangbao may reduce the level of BACE1 by lowering blood sugar. Current research shows that blood sugar levels may have an impact on BACE1. Hyperglycemic states may affect the expression and activity of BACE1 through multiple pathways. For example, long-term hyperglycemia may trigger oxidative stress and inflammatory responses, thereby activating certain cellular signaling pathways and leading to increased expression of BACE1. In addition, metabolic disorders caused by hyperglycemia may affect the energy balance and material metabolism in cells and indirectly regulate the function of BACE1. However, the specific influence mechanism is not completely clear, and more in-depth research is still needed to clarify the complex relationship between blood sugar and BACE1.

5. Conclusions

In summary, aluminum maltol poisoning affects the expression level of β-site amyloid precursor protein cleaving enzyme 1 (BACE1), causes the accumulation of β-amyloid protein, and then destroys its learning and memory ability. Guangxi sweet tea and Shutangbao regulate the expression of BACE1 by lowering blood sugar. Therefore, for the treatment of diabetes and Alzheimer's disease, we have a new treatment direction. We can remove aluminum or intervene in the

accumulation of β-amyloid protein and remove β-amyloid protein precipitation, etc., providing an innovation point for the prevention and treatment of Alzheimer's disease in the future and showing new hope for reducing the population of Alzheimer's disease patients all over the world. However, its more specific and detailed mechanism will need to be further studied in the future.

Acknowledgement

Innovative training project on exploring the pathogenesis of type 2 senile diabetes modeled by streptozotocin with sweet tea. National level. Number: 202410599019.

References

[1] Zhu Xiaoying, Huang Guangyan, Li Qiuping, Huang Lingling, Tao Jiying, Zhang Shuqiu. Observation on the effect of Shutangbao oral liquid in treating type 2 diabetic mouse models[J]. Guangxi Medical Journal, 2013, 35(01):35-37.
[2] Zuo Pingping. Metabolism of β-amyloid peptide and Alzheimer's disease[J]. Labeled Immunoassays and Clinical Medicine, 2001(01):34-37.
[3] Postina R. A closer look at α-secretase[J]. Curr Alzheimer Res, 2008, 5(2):179-186.
[4] Wang Yuechun, Wang Zidong, Sun Liming, He Sichun, Bai Zhiquan. Y-maze test method for animal learning and memory ability (review)[J]. Journal of Jinan University (Natural Science and Medicine Edition), 2001(05):137-140.
[5] Liu Junhui, Zhou Xiaolei, Weng Mingzuan, Wang Shuo. Hypoglycemic effect of Guangxi sweet tea polyphenols on alloxan-induced diabetic mice[J]. Pharmacology and Clinics of Chinese Materia Medica, 2014, 30(06):51-54. DOI:10.13412/j.cnki.zyyl.2014.06.016.
[6] Cheng Xiaolin, Yu Qingjiang, Wang Jiazhu. Harm of aluminum to human health and prevention and treatment[J]. Journal of Heze Teachers College, 2004(04):57-60. DOI:10.16393/j.cnki.37-1436/z.2004.04.016.
[7] Tadahiro K. The role of FOXO1 in β-cell failure and type 2 diabetes mellitus.[J]. Nature reviews. Endocrinology, 2013, 9(10):615-623.
[8] Li Fengling, Long Qijun, Wei Aibo, et al. Effect of Shutangbao on blood glucose in alloxan-induced diabetic mice[J]. Journal of Youjiang Medical University, 2009, 31(02):162-164.
[9] Castorina Alessandro et al. Early effects of aluminum chloride on beta-secretase mRNA expression in a neuronal model of beta-amyloid toxicity. [J]. Cell biology and toxicology, 2010, 26(4):367-377.
[10] Luo Y, Niu F, Sun Z, et al. Altered expression of Abeta metabolism-associated molecules from D-galactose/ AlCl(3)induced mouse brain. Mech Ageing Dev, 2009, 130(4):248-252.
[11] Fiorelli T, Kirouac L, Padmanabhan J. Altered processing of amyloid precursor protein in cells undergoing apoptosis [J]. PloS one, 2013, 8(2):57979.