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Penulis : Reza Mahendra, Ainul Rofik, Hotimah Masdan Salim, Maria Ulfa, Evi Sylvia Awwalia

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Achmad Syafiuddin, Ph.D.

NPP. 20071300

LPPM Universitas Nahdlatul Ulama Surabaya

Website : lppm.unusa.ac.id

Email : lppm@unusa.ac.id

Hotline : 0838.5706.3867

Neuroprotective activity of extract of celery (*Apium graveolens*) in insilico study

by MariaUlfa

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ORIGINAL ARTICLE

NEUROPROTECTIVE ACTIVITY of EXTRACT of CELERY (*APIUM GRAVEOLENS*) IN INSILICO STUDY

Reza Mahendra Putra¹, Ainul Rofik¹, Hotimah Masdan Salim², Maria Ulfa³, Evi Sylvia Awwalia⁴

¹ Department of Anesthesiology and Intensive Therapy Faculty of Medicine, Universitas Nahdlatul Ulama Surabaya, Surabaya, Indonesia

² Department of Biochemistry and Biomolecular Science, Faculty of Medicine, Universitas Nahdlatul Ulama Surabaya, Surabaya, Indonesia

³ Department of Dermatology and Venereology, Faculty of Medicine, Universitas Nahdlatul Ulama Surabaya, Surabaya, Indonesia

⁴ Department of Internal Medicine, Faculty of Medicine, Universitas Nahdlatul Ulama Surabaya, Surabaya, Indonesia

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*) Correspondent author:
dr.reza@unusa.ac.id

ABSTRACT

Background: Celery (*Apium graveolens* L., *Apiaceae*) is one of the medicinal plants with secondary metabolite components that have pharmacological effects such as vitamin (choline) content. This study aims to evaluate the mechanism and interaction of choline contained in celery on its effectiveness as a neuroprotective.

Methods: This research is an experimental research using the in silico study.

Results: The insilico search found that the choline content in celery binds to Slc5a7, Chat and Ache. Which has a function in the process of neurotransmitter biosynthesis, neurotransmitter metabolic processes and neurotransmitter secretion processes

Conclusion: The celery (*Apium graveolens* L., *Apiaceae*) have pharmacological activity as neuroprotective through the interaction of Slc5a7, Chat and Ache.

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Introduction

The use of herbal plants in medicine has been used for centuries and until now, herbal medicine has shown pharmacological activity which is quite effective in various diseases^{1,2}.

One of the herbal plants that are often used in medicine is celery. *Apium graveolens* or celery belongs to the Apiaceae family. Celery plants grow throughout the continent of Asia, Europe, and parts of Africa that have a tropical climate, but until now celery has been consumed and cultivated throughout the world³.

Previous pharmacological studies have shown that celery has antimicrobial activity, antiparasitic, cardioprotective, gastroprotective, neuroprotective, hypolipidemic, cytotoxic, antioxidant, anti-inflammatory, and antiinfertility⁴⁻⁶. Until now, the public's knowledge in using celery is still limited as a flavor enhancer for food and vegetable commodities.

The methanol extract of the celery seeds contains several chemical compounds of flavonoids, steroids, glycosides, and alkaloids Celery also contains furocoumarins, phenols, sesquiterpenes alcohol, and essential oils^{7,8}.

Recent research has also shown that celery contains vitamins (choline and riboflavin), and pigments (safflomin A)⁹.

There are so many benefits of celery, but very little has been explained about the benefits of celery on the nervous system. Although previous studies have found the effect of celery as a neuroprotective, but its mechanism is still not widely known. So, the study aims to determine the mechanism of the vitamin content, namely choline in celery leaves on the function of the nervous system, especially neurotransmitters in-silico.

Methods

This type of research is experimental research in silico. Components of secondary metabolites in celery based on previous research⁹.

The secondary metabolite in celery used in the insilico search is vitamin (choline). Then the search for choline interactions with proteins is carried out in the following way:

1. Search for secondary metabolites (choline) by accessing <https://pubchem.ncbi.nlm.nih.gov/>
 2. Searching for choline interactions with proteins in the body by accessing <http://stitch.embl.de> and continued by looking at the structure of each protein from the Protein data bank (PDB) <http://rcsb.org>
 3. Then search for specific functions based on the interaction of each protein by accessing <https://string-db.org/>.
-

Results

From the results of an insilico search for the metabolite content of celery, namely choline, a 3D structure was obtained through a search on Pubchem as shown in Figure 1.

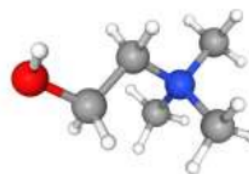


Figure.1 The 3D picture of Choline structure

After determining the chemical structure of choline based on the canonical smile, the search for choline interactions in the body was carried out using the stitch.embl.de database. The search found strong interactions of choline on Slc5a7, Chat, and Ache proteins where these three proteins function at cholinergic synapses (neurotransmitters) (figure.2)

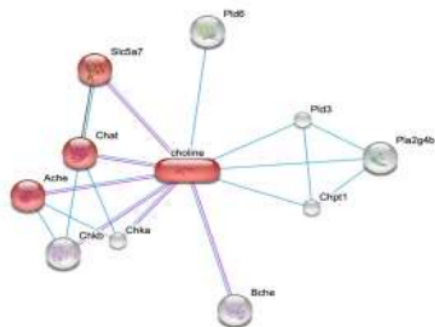


Figure.2 Prediction of coline interactions on proteins in the body

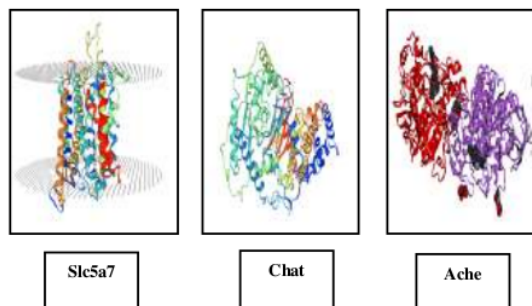


Figure.3 The 3D picture of each protein

To find out the specific function of each protein, a search was carried out through the data base accessed at <https://string-db.org/>. From the search results, it was found that the three proteins have more than one function, namely the process of neurotransmitter biosynthesis, metabolic neurotransmitter processes, neurotransmitter secretion processes and metabolic hormone processes (Figure.4)

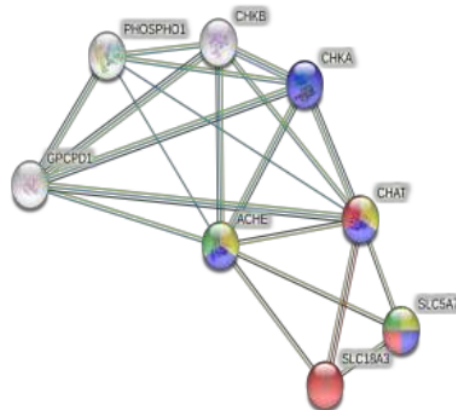


Figure.4 Interaction function of Chat, ACHE, SLC5A7

Table.1 The function of protein in nervous systems

Function	Protein	Indication
Neurotransmitter biosintetic process	1. Chat	Yellow
	2. ACHE	
	3. SLC5A7	
Neurotransmitter metabolic process	1. CHKA	Purple
	2. CHAT	
	3. ACHE	
	4. SLC5A7	
Secretion neurotransmitter	1. CHAT	Red
	2. SLC18A3	
	3. SLC5A7	
Hormon metabolic process	1. ACHE	Green
	2. SLC5A7	

Discussion

This study evaluates the content of secondary compounds from celery extract, namely choline as a neuroprotective with an in silico approach. The approach was taken by looking at the interaction of Colin from celery extract on proteins in the body. Based on the results of this study, it was found that there are three proteins that have strong interaction

with choline which is a secondary metabolite component of celery, namely Slc5a7, Chat, and Ache, which work specifically on neurotransmitters in the nervous system. These results are in line with previous studies, which found that celery extract has a neuroprotective effect, although the mechanism has not yet been clearly explained¹.

The results of this study can be one of the initial data for interactions related to the mechanism of celery in providing a neuroprotective effect.

This study was found that Slc5a7, Chat, and Ache have interactions in the process of neurotransmitter biosynthesis, neurotransmitter metabolic process, secretion of neurotransmitter, and hormone metabolic process. These three proteins assist in the transmembrane transporter that imports choline from the extracellular space into high-affinity neurons. Choline absorption is the rate-limiting step in acetylcholine synthesis¹⁰.

Previous studies have found that mutations in Slc5a7 are found in a rare group of genetically heterogeneous neuromuscular junction (NMJ) disorders associated with variable skeletal muscle fatigue and weakness, generally classified under the term 'congenital myasthenic syndrome' (CMS)¹¹. Other studies have found that Slc5a7 also has a role in the process of Alzheimer's disease (AZ)¹².

It is well known that the enzyme choline acetyltransferase (Chat) catalyzes the transfer of an acetyl group from acetyl-coenzyme A (acetyl-CoA) to choline to produce ACh in the axoplasm of neurons. After its biosynthesis, ACh is packaged into synaptic vesicles by the vesicular ACh transporter (VACHT) and released into the synaptic cleft upon neuronal depolarization. This ACh then

binds to nicotinic and muscarinic receptors to activate downstream signaling pathways, then the transmitter is broken down by the enzyme acetylcholinesterase (AChE) into acetate and choline to limit its binding to the receptor. these two proteins are essential in the process of signaling via neurotransmitters in a variety of biological processes, including cognition, movement, and attention processing¹³.

The interactions obtained in the insilico can be used as a reference in knowing the mechanism of the secondary metabolite of celery extract, namely choline and it can be suggested to use celery as a medicinal plant that has a neuroprotective effect.

Conclusion

Apium graveolens or celery belongs to the Apiaceae family. Based on the results of an insilico search for the content of secondary metabolites, namely choline, that celery leaves have pharmacological activity as neuroprotective through the interaction of SLC5a7, ChAt, and Ache and suggested as a very potential medicinal plant. However, a number of studies are still needed to validate the effectiveness of celery as a treatment.

Conflict Of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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