



INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES

Published by JK Welfare & Pharmascope Foundation

Journal Home Page: <https://ijrps.com>

Acetylcholinesterase inhibitory effect of capsicum oleoresins – an *in vitro* study

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Article History:

Received on: 28.06.2018
Revised on: 21.08.2018
Accepted on: 25.08.2018

Keywords:

Acetylcholine esterase,
Inhibitory effect,
Alzheimer's disease,
Capsicum oleoresins

ABSTRACT

The present study aimed to evaluate the acetylcholine esterase inhibitory effect of capsicum oleoresin. Capsicum extract were examined for their AChE inhibitory activities at different concentrations (10, 20, 40, 60, 80, 100, 120 and 140µg/ml) spectrophotometrically. The extract was dissolved in a base-tris (0.05 M) buffer. In this method, 200µl of acetylthiocholine iodide (15mM), 1000µl of DTNB (3mM), and 200µl of test extract solution at the different concentrations were mixed and incubated for 15 min at 30°C. Then, the mixture was monitored spectrophotometrically at 412 nm 10 times, each 13 s. After that, 200µl of AChE (0.3U/ml) solution were added to the initial mixture, to start the reaction and then the absorbance was determined. Minimum inhibition of 7.2 ±0.37% at 10µg/ml and maximum inhibition of 78.26 ±1.26% at 140µg/ml was exhibited. The IC₅₀ was found to be 68.28µg/ml. Capsicum oleoresin at different concentrations showed a dose-dependent decrease in AChE activity which was promising to suggest it as a candidate for the management of Alzheimer's after further validation as it can increase the availability of acetylcholine.



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inability to learn new information, mood swings, difficulty in finding words, forgetting names, and losing items are the early symptoms. Frustration, hostility, and irritability are common emotional features exhibited by patients with AD (Rao *et al.* (Murray *et al.*, 2013). Loss of short-term memory,

ISSN: 0975-7538

DOI: <https://doi.org/10.26452/ijrps.v9i4.1645>

Production and Hosted by

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INTRODUCTION

Alzheimer's disease (AD) is one of the most common types of dementia associated with old age. Scientific data from WHO estimate around 35.6 million people living with dementia worldwide and expect it to double by 2030 and triple by 2050 (Hung *et al.*, 2016) Alzheimer's is a progressive neurodegenerative disorder associated with memory impairment and cognitive deficit with low levels of acetylcholine in the brain

2012). One of the significant ways to treat the disease is by enhancing acetylcholine levels in the brain (Adewusi *et al.*, 2011). The current drugs used against AD are plant-derived alkaloids: rivastigmine and galantamine. (Machado *et al.*, 2015). Acetylcholine plays a vital role in cognitive function including learning and memory and is evident that the anticholinesterase (AChE) activity has memory enhancing properties (Divya *et al.*, 2014). Hence, AChE inhibition is considered as a promising therapeutic strategy for other types of dementia, myasthenia gravis, glaucoma and Parkinson's disease and AD (Mehta *et al.*, 2012). Acetylcholinesterase inhibitors are associated with many side effects such as anorexia, diarrhoea, fatigue, nausea, muscle cramps as well as gastrointestinal, cardiorespiratory, genitourinary and sleep disturbances (Chattipakorn *et al.*, 2007). Hence, there is a need for exploring the nature for

newer potent and long lasting AChE inhibitors with minimal side effects. Many plants are explored for their inhibitory effect on acetylcholinesterase and thereby their use in Alzheimer's. (Anitha Roy *et al.*, 2011; Shekarchi *et al.*, 2013; Hajimehdipoor, 2013; Soodi *et al.*, 2014)

Capsicum oleoresin was used for the study was isolated from *Capsicum annuum* (family *Solanaceae*). Capsicum oleoresin contains capsaicin. Capsaicin has excellent potential for promoting vascular and metabolic health. Capsaicin boosts metabolic rate modestly and its transdermal patch, increase exercise time to an ischaemic threshold in patients with angina. (McCarty *et al.*, 2015). Here in this study, the capsicum oleoresin was evaluated for its acetylcholinesterase inhibitory property.

MATERIALS AND METHOD

Chemicals and plant extract

Tris buffer, acetylthiocholine iodide, 5,5'-dithiobis nitrobenzoic acid (DTNB). Capsicum oleoresin was obtained from Synthite Industries Ltd, Kerala as gratis.

In vitro acetylcholinesterase (AChE) inhibition assay

Capsicum extract were examined for their AChE inhibitory activities at different concentrations (10, 20, 40, 60, 80, 100, 120 and 140 µg/ml) and were dissolved in a base-tris (0.05 M) buffer, following the spectrophotometric method developed by Ellman *et al.* (1961) as described by Salles *et al.* (2003). In this method, 200 µl of acetylthiocholine iodide (15mM), 1000 µl of DTNB (3mM), and 200 µl of test extract solution at the different concentrations were mixed and incubated for 15 min at 30°C. Then, the mixture was monitored spectrophotometrically at 412 nm 10 times, each 13 s. After that, 200 µl of AChE (0.3U/ml) solution were added to the initial mixture, to start the reaction and then the absorbance was determined. The control contained all components except the tested extract. All treatments were performed in triplicate with two replicates. The percentage of AChE inhibitory activity (% IA) was calculated by using the following equation:

$$IA (\%) = \frac{(\text{Activity of Control} - \text{Activity of Test})}{\text{Activity of Control}} \times 100$$

Estimation of IC₅₀ values

The concentrations of the tested extract that inhibited the hydrolysis of acetylthiocholine by 50% (IC₅₀) were determined by a linear regression analysis between the inhibition percentages

against the extract concentrations by using the Graph pad prism.

RESULTS AND DISCUSSION

Capsicum extract at different concentrations was evaluated for its inhibitory effect on the acetylcholinesterase activity. A concentration-dependent decrease in AChE activity was observed for all the tested concentrations of capsicum oleoresin. Minimum inhibition of $7.2 \pm 0.37\%$ at 10 µg/ml and maximum inhibition of $78.26 \pm 1.26\%$ at 140 µg/ml was exhibited. The IC₅₀ was found to be 68.28 µg/ml (figure 1)

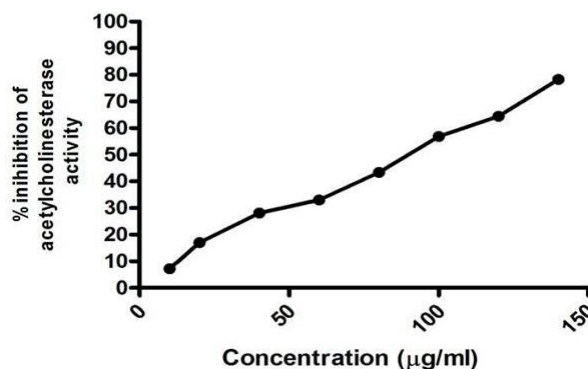


Figure 1: Inhibitory effect of capsicum oleoresin on acetylcholine esterase

The study has proved the dose-dependent inhibitory effect of capsicum oleoresin on AChE. It showed maximum inhibition of $78.26 \pm 1.26\%$ at 140 µg/ml was exhibited. The IC₅₀ was found to be 68.28 µg/ml. Hence, capsicum oleoresin may be used for enhancing the availability of acetylcholine in conditions such as Alzheimer's disease.

The cholinergic deficit is found to be the consistent and early finding in Alzheimer's disease. Hence, acetylcholinesterase was found to be the most viable therapeutic target for symptomatic improvement in Alzheimer's disease (Mehta *et al.*, 2012). Acetylcholinesterase hydrolyses ACh to choline and acetate, thereby terminating the effect of Ach at cholinergic synapses. Hence, AChE is the target of cholinesterase inhibitors used to address the cholinergic deficit in Alzheimer's disease patients. (Ranjan and Kumari., 2017). Plants with anticholinesterase activity may have a favourable pharmacological profile in the treatment of Alzheimer's disease. Natural products are promising sources of acetylcholinesterase inhibitors (Murray *et al.*, 2013). Researchers have proved that secondary metabolites such as flavonoids and phenolic compounds can inhibit AChE and could be useful in the treatment of AD. (Uriarte – Pueyo *et al.*, 2011).

Oleoresin of capsicum used for the study contains capsaicin which is a capsaicinoid. Capsaicinoids are gaining attention as a nutraceutical health

supplement today with a wide variety of health benefits (Sandya and Trupti 2017). Capsaicinoids have antioxidant activity because of the presence of the phenolic ring in them. (Mitic *et al.*, 2018; Viktorija *et al.*, 2014) Studies have proven the merits of capsaicin in clinical evaluation for endothelial function, the progression of atherosclerosis in diabetics, angina, non-alcoholic fatty liver disease, cardiac hypertrophy, metabolic syndrome, hypertension, obesity and gastric ulceration. It can inhibit gastric acid secretion, boost secretion of alkali and mucous, and stimulate gastric blood flow. (Mc Carty *et al.*, 2015). Capsaicin being one of the versatile phytochemicals, positively its anticholinesterase inhibitory effect of capsicum oleoresin will contribute to the scientific community for further investigation for its use in Alzheimer's.

CONCLUSION

AChE inhibitory activity is promising to suggest that capsicum oleoresin is a good candidate for the management of Alzheimer's after further validation as it can increase the availability of acetylcholine. Moreover, compounds with AChE inhibitory effect may also be used for the treatment of senile dementia, myasthenia gravis, Parkinson's disease and ataxia.

Conflict of Interest

Authors declare no conflict of interest

Acknowledgement

The authors thank Synthite Industries Ltd, Kerala for providing capsicum oleoresin as a gift sample and also express their gratitude to Ms. Parameshwarari P.R Senior Research fellow, SRMC, Chennai for interpreting the results.

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