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The beneficial role of apigenin against cognitive dysfunction and neurobehavioural deficit: A Protocol of Systematic review

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 02 December 2023 and was last updated on 02 December 2023.

INTRODUCTION

Review question / Objective Can apigenin improve cognitive dysfunction and neurobehavioural impairment in animal model of neurodegenerative diseases?

Rationale Neurodegenerative diseases have been linked to an increase in the aging population. Most neurodegenerative diseases, such as Alzheimer's disease (AD), Parkinson's disease (PD) and multiple sclerosis, are associated with cognitive and neurobehavioural changes. The degeneration of neurons, which may be caused by intrinsic or extrinsic factors, may trigger processes that lead to cognitive decline and neurobehavioural impairment. The progression of degeneration and loss of neurons is characterized by memory loss, impaired recognition and working memory, learning abilities, motor dysfunction, anxiety and depression.

Several therapeutic strategies have been developed to treat the symptoms and mitigate the progression of these impairments to improve the quality of life. While some synthetic compounds have shown promising and effective therapeutic strategies, their side effects have been a major limitation for the usage of these drugs. Moreover, the use of natural compounds has shown promising results for the treatment of neurological diseases. The impact of flavonoids on neurological function has been studied extensively. This class of polyphenols has shown potent neuroprotective effects against some neurodegenerative diseases in different experimental models.

Apigenin is a flavone-kind of flavonoid present in fruits, teas, and vegetables. It is a potent antioxidant and has been shown to exhibit anti-inflammatory, antitumorigenic and antimicrobial activities. Its ability to cross the blood-brain barrier is important as it contributes to its pharmacological activity against neurological

disorders. Apigenin exhibited a neuroprotective effect against peripheral nerve degeneration. Some studies have also established that apigenin confers antidepressant activity, mediated by its effect on α-adrenergic, dopaminergic, and serotonergic receptors. Apigenin improved serotonin, dopamine and epinephrine levels, which were altered in depressive animals. Some experimental evidence and expert reviews have shown the pharmacological activities of apigenin, especially against some neurological diseases. However, no systematic review has assessed the effect of apigenin on cognitive dysfunction and neurobehavioural deficit in preclinical models. Hence, this study sought to assess the effect of apignin on learning and memory, sensorimotor function, motor coordination, anxiety-like behaviour and depressive-like behaviour. The results of this study will reveal the gaps in current and previous evidence and provide information for future studies and possible exploration of apigenin in clinical studies.

Condition being studied Cognitive dysfunction and neurobehavioural deficit in stressed or chemical – induced neurodegeneration in animal model.

METHODS

Search strategy The following search terms were used: “Apigenin AND (memor* OR cogniti* OR *behav* OR neuroinflammati* OR neurodegenerat* OR Alzheim* OR Parkinso*).

Participant or population Animals (rodents [rat or mice]) induced with cognitive impairment or neurobehavioural and treated with apigenin versus control animals with cognitive impairment and neurobehavioural deficit without treatment with apigenin.

Intervention Any dosage of apigenin administered for any duration to animals induced with cognitive impairment and neurobehavioural deficit, which is confirmed using different cognitive and neurobehavioural paradigms.The use of Apigenin.

Comparator A group of rats or mice induced cognitive impairment and neurobehavioural dysfunction.

Study designs to be included Preclinical studies or animal studies that used mouse or rat; studies that used any dosage of apigenin administered for any duration versus control group treated with stress or any chemical capable of inducing memory deficit or neurobehavioural dysfunction (2) that they measured outcomes that focused on memory and learning using Morris water Maze, Barnes Maze, Y-Maze, T-Maze, Novel object recognition, Passive avoidance test, inhibitory avoidance, anxiety-like behaviour (elevated plus maze, dark-light model of anxiety), depressive-like behaviour (forced swimming test, sucrose preference test, t.

Eligibility criteria Articles that report plant extract containing apigenin or mixtures of apigenin with other compounds will not be included. Studies involving the use of Caenorhabditis elegans and Drosophila melanogaster and other models will not rat or mouse model will not be accepted.

Information sources Scopus, PubMed, Google Scholar and Web of Science.

Main outcome(s) With respect to types of outcome measure, our analysis will focus on indices and task performance, or paradigms associated with learning and memory, anxiety-like behaviour, depressive-like behaviour, locomotor behaviour, and sensorimotor and motor coordination.

Quality assessment / Risk of bias analysis Quality assessment will be carried out using The 3-category Scottish Intercollegiate Guidelines Network (SIGN) grading system to evaluate the quality of each article included in the study. Each article was screened for high quality, acceptable, and unacceptable based on the set criteria. Articles that meet all the criteria after assessment are of high quality. If each article meets most criteria, it will be graded as acceptable. Unacceptable articles do not meet most of the outlined criteria.The method of assessment will be carried out using the.

Strategy of data synthesis The data synthesis will involve qualitative synthesis.

Subgroup analysis Sub-group analysis is not intended in this study.

Sensitivity analysis The impact of arbitrary decisions on the screened articles will be explored.

Language restriction Only Preclinical or in vivo model involving rodents (rat or mouse) published in English will be considered for inclusion.

Country(ies) involved South Africa and Nigeria.

Keywords Cognitive impairment; Neurobehavioural deficit, Neurodegenerative disease; Learning and Memory.

Contributions of each author

Author 1 - Tosin Olasehinde - Conceptualized the study, carried out preliminary search and screening, data extract, data synthesis, Drafted the manuscript.
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Author 2 - Oyiinlola Olaokun - Carried out screening for inclusion, data synthesis, qualitative synthesis, proofread manuscript.
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