

A Systematic Review of the Capsaicin and other TRPV1 agonists effects on three neurodegenerative diseases: Alzheimer's disease, Parkinson's disease and Ischemic Stroke

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ADMINISTRATIVE INFORMATION**Support** - None.**Review Stage at time of this submission** - Preliminary searches.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202440115**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 April 2024 and was last updated on 28 April 2024.**INTRODUCTION**

Review question / Objective What are the mechanisms of capsaicin and other TRPV1 agonists in three animal models of neurodegenerative diseases? Animal models of neurodegenerative diseases were treated with capsaicin and other TRPV1 agonists, compared with the control group (Purified water-treated, saline-treated, conventional therapy or no treatment), observed behavioral changes and detected changes in Infarction volume, DA levels, β amyloid and tau protein, explaining the mechanism of action.

Condition being studied Neurodegenerative diseases (NDDs) are a group of neurological disorders characterized by progressive neuronal loss in the central nervous system (CNS) or peripheral nervous system (PNS). Ischemic stroke is a disease that causes hypoxia, ischemia, and necrosis of brain tissue due to obstruction of cerebral blood flow. Ischemic stroke can lead to sudden neurological damage, such as limb

paralysis, language impairment, and cognitive dysfunction. Parkinson's disease (PD) is a neurodegenerative disorder characterized by the degeneration and loss of dopamine neurons in the central nervous system. This degeneration leads to motor dysfunction such as muscle stiffness, tremor, and bradykinesia. Alzheimer's disease (AD) is one of the most common neurodegenerative disorders, mainly affecting the elderly. The disease causes the degeneration and death of nerve cells in the brain, ultimately leading to the loss of cognitive function.

METHODS

Search strategy TS=(Capsaicin OR capsaicin OR 8-Methyl-N-Vanillyl-6-Nonenamide OR 8 Methyl N Vanillyl 6 Nonenamide OR antiphlogistique rub A-535 Capsaicin OR Axsain OR zakin OR capsidiol OR Zostrix OR Capzasin OR geloen OR atrum OR NGX-4010 OR NGX 4010 OR NGX4010 OR capsicum farmaka OR capsid OR Evodiamine OR Dihydrocapsaicin OR Capsiate OR MDR-652 OR Rinvanil OR MSP-3 OR (R)-Methanandamide OR

N-Arachidonyldopamine OR Dihydrocapsiate) AND TS=(Ischemic Stroke OR Ischemic Strokes OR Stroke, Ischemic OR Ischaemic Stroke OR Ischaemic Strokes OR Stroke, Ischaemic OR Cryptogenic Ischemic Stroke OR Cryptogenic Ischemic Strokes OR Ischemic Stroke, Cryptogenic OR Stroke, Cryptogenic Ischemic OR Cryptogenic Stroke OR Cryptogenic Strokes OR Stroke, Cryptogenic OR Cryptogenic Embolism Stroke OR Cryptogenic Embolism Strokes OR Parkinson Disease OR Idiopathic Parkinson's Disease OR Lewy Body Parkinson's Disease OR Parkinson's Disease, Idiopathic OR Parkinson's Disease, Lewy Body OR Parkinson Disease, Idiopathic OR Parkinson's Disease OR Idiopathic Parkinson Disease OR Lewy Body Parkinson Disease OR Primary Parkinsonism OR Parkinsonism, Primary OR Paralysis Agitans OR Alzheimer's disease OR Alzheimer Dementia OR Alzheimer Dementias OR Dementia, Alzheimer OR Alzheimer's Disease OR Dementia, Senile OR Senile Dementia OR Dementia, Alzheimer Type OR Alzheimer Type Dementia OR Alzheimer-Type Dementia OR Alzheimer Type Dementia OR Dementia, Alzheimer-Type OR Alzheimer Type Senile Dementia OR Primary Senile Degenerative Dementia OR Dementia, Primary Senile Degenerative OR Alzheimer Sclerosis OR Sclerosis, Alzheimer OR Alzheimer Syndrome OR Alzheimer's Diseases OR Alzheimer Diseases OR Alzheimers Diseases OR Senile Dementia, Alzheimer Type OR Acute Confusional Senile Dementia OR Senile Dementia, Acute Confusional OR Dementia, Presenile OR Presenile Dementia OR Alzheimer Disease, Late Onset OR Late Onset Alzheimer Disease OR Alzheimer's Disease, Focal Onset OR Focal Onset Alzheimer's Disease OR Familial Alzheimer Disease OR Alzheimer Disease, Familial OR Familial Alzheimer Diseases OR Alzheimer Disease, Early Onset OR Early Onset Alzheimer Disease OR Presenile Alzheimer Dementia) Four English databases including PubMed, Scopus, Web of Science, Embase and four Chinese databases including China National Knowledge Infrastructure (CNKI), Wanfang Data knowledge service platform, the Chinese Scientific Journals Full-text Database (VIP) and China biomedical literature service system (SinoMed) will be searched without language limitation. The combination of MeSH terms and free words will be adopted by us for database searching.

Participant or population Animal models of Neurodegenerative diseases. The methods for inducing Neurodegenerative diseases animal models are not limited. The species of animal is restricted to rats or mice or flies. The sex of the animal is not limited.

Intervention Capsaicin and other TRPV1 agonist. All doses, duration and administration methods were not limited.

Comparator Purified water-treated, saline-treated, conventional therapy or no treatment.

Study designs to be included Controlled studies with separate treatment groups.

Eligibility criteria Only full-text publications in English and Chinese will be included, with no date limitations. Abstracts, review articles, letters, editorials, unpublished grey literature, studies involving solely in vitro or ex vivo data and duplicate publication will be excluded.

Information sources Four English databases including PubMed, Scopus, Web of Science, Embase and four Chinese databases including China National Knowledge Infrastructure (CNKI), Wanfang Data knowledge service platform, the Chinese Scientific Journals Full-text Database (VIP) and China biomedical literature service system (SinoMed).

Main outcome(s) Inclusion criteria: 1) Behavioral and cognitive abilities 2) Infarction volume, DA levels, β amyloid and tau protein 3) mechanism: the levels of inflammatory mediators such as IL-1 β , TNF- α , and IL-6 inflammation-related protein/gene expression oxidative stress. Neuroprotective mechanisms such as induced hypothermia and cell apoptosis.

Quality assessment / Risk of bias analysis By using SYRCL's risk-of-bias tool.

Strategy of data synthesis One investigator will search studies in those databases and list the titles and abstracts of all articles. Two reviewers will read the title and abstract of all articles and select eligible articles independently according to inclusion and exclusion criteria. Reviewers will download articles and read full text when decisions cannot be made according to the titles and abstracts. Disagreements would be discussed with a third reviewer. Two reviewers will independently extract the text of each study from the included studies using a standardized checklist. Any discrepancy will be resolved by discussion with a third reviewer. In the included research, we will extract the data in the text and table. Authors will be contacted to provide missing or additional data by email.

Subgroup analysis Not planned.

Sensitivity analysis Not planned.

Country(ies) involved China.

Keywords Neurodegenerative diseases; Ischemic stroke; Parkinson disease; Alzheimer's disease; capsaicin; TRPV1 agonist.

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