# Histamine H3 inverse agonist BF 2649 or antagonist with partial h4 agonist activity clobenpropit reduces amyloid beta peptide-induced brain pathology in alzheimer?s disease

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Alzheimer?s disease (AD) is one of the leading causes for disability and death affecting millions of people worldwide. Thus, novel therapeutic strategies are needed to reduce brain pathology associated with AD. In view of increasing awareness regarding involvement of histaminergic pathways in AD, we explored the role of one H3 receptor inverse agonist BF 2649 and one selective H3 receptor antagonist with partial H4 agonist activity in amyloid beta peptide (A?P) infusion-induced brain pathology in a rat model. AD-like pathology was produced by administering A?P (1?40) intracerebroventricular (i.c.v.) in the left lateral ventricle (250 ng/10 ?l, once daily) for 4 weeks. Control rats received saline. In separate group of rats, either BF 2649 (1 mg/kg, i.p.) or clobenpropit (1 mg/kg, i.p.) was administered once daily for 1 week after 3 weeks of A?P administration. After 30 days, blood-brain barrier (BBB) breakdown, edema formation, neuronal, glial injuries, and A?P deposits were examined in the brain. A significant reduction in A?P deposits along with marked reduction in neuronal or glial reactions was seen in the drug-treated group. The BBB breakdown to Evans blue albumin and radioiodine in the cortex, hippocampus, hypothalamus, and cerebellum was also significantly reduced in these drug-treated groups. Clobenpropit showed superior effects than the BF2649 in reducing brain pathology in AD. Taken together, our

observations are the first to show that blockade of H3 and stimulation of H4 receptors are beneficial for the treatment of AD pathology, not reported earlier. 

Alzheimer?s disease (AD)

Amyloid beta peptide (A?P)

BF2649

Blood-brain barrier

Brain pathology

Clobenpropit

H3 receptor inverse agonist

H3 receptors antagonist with partial H4 agonist

Histamine

albumin

amyloid beta protein[1-40]

bf 2649

clobenpropit

glial fibrillary acidic protein

histamine H3 receptor agonist

radioactive iodine

unclassified drug

amyloid beta protein

clobenpropit

histamine agonist

histamine H3 receptor antagonist

histamine H4 receptor

Hrh4 protein, rat

imidazole derivative

thiourea

Alzheimer disease

animal cell

animal experiment

animal model

animal tissue

Article

blood brain barrier

brain cortex

brain edema

brain nerve cell

cell damage

cerebellum

controlled study

drug effect

glia cell

hippocampus

histopathology

hypothalamus

immunohistochemistry

lateral brain ventricle

male

nonhuman

rat

agonists

Alzheimer disease

analogs and derivatives

animal

brain

chemically induced

inverse agonism

partial agonism

pathology

Sprague Dawley rat

Alzheimer Disease

Amyloid beta-Peptides

Animals

Brain

Drug Inverse Agonism

Drug Partial Agonism

Histamine Agonists

Histamine H3 Antagonists

Imidazoles

Male

Rats

Rats, Sprague-Dawley

Receptors, Histamine H4

Thiourea