Amelioration of Neuropathology by a Novel Extract of *Nerium Oleander* in APP/PSEN1dE9 transgenic mouse

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ABSTARCT

There have been numerous efforts for the development of the therapy for Alzheimer's disease (AD) although effective treatment is not still available. PBI-05204, the botanical extract of *Nerium oleander,* has been shown to have neuroprotective effects in rodent models of stroke. Both Oleanolic acid and triterpenoids, the main constituent of this extract, have been shown to modulate multiple cellular pathways including oxidative stress, inflammation, proliferation and apoptosis, all of which have been shown to be pathologically linked with AD, supporting the therapeutic potential of PBI-05204 for the treatment of AD. To test the therapeutic potential, we treated APP/PSEN1dE9 mice with PBI-05204 or vehicle for 4 months (4-8 months of age) and examined its effect on AD-related neuropathology. In our analysis, we found that Aβ plaques were significantly reduced by the treatment of PBI-05204 compared to control mice. Furthermore, the treatment with PBI-05204 significantly reduced neuroinflammation which is evidenced by the reduced activation of microglia and astrocytes. Collectively, our data clearly indicates that the treatment of PBI-05204 reduces amyloid pathology and neuroinflammation in APP/PSEN1dE9 transgenic mouse model, suggesting the therapeutic potential of PBI-05204 for the treatment of AD.

INTRODUCTION

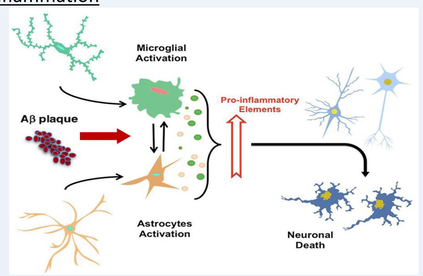
NERIUM OLEANDER

Supercritical CO_2 extract → PBI-05204

Previously reported to display neuroprotective activity in stroke

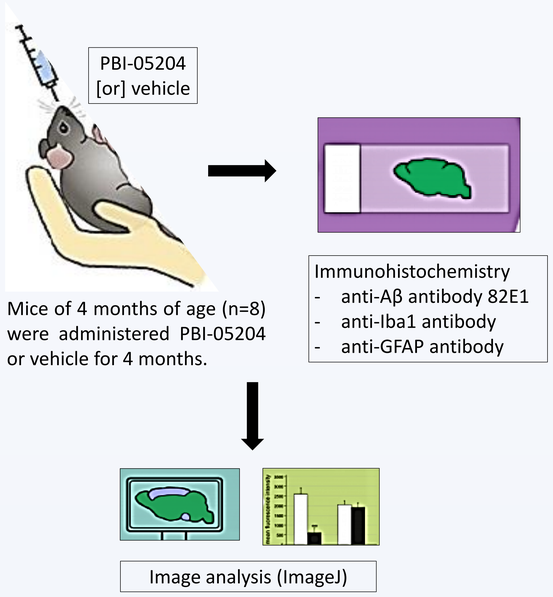
APP/PSEN1dE9 double transgenic mouse model develops AD-like neuropathology, including amyloid plaques and gliosis around 4 months of age.

Neuroinflammation



To investigate the effects of PBI-05204 on neuroinflammation in the APP/PSEN1 mouse model, we will investigate the distribution of astrocytes and microglia.

MATERIALS & METHODS



RESULTS

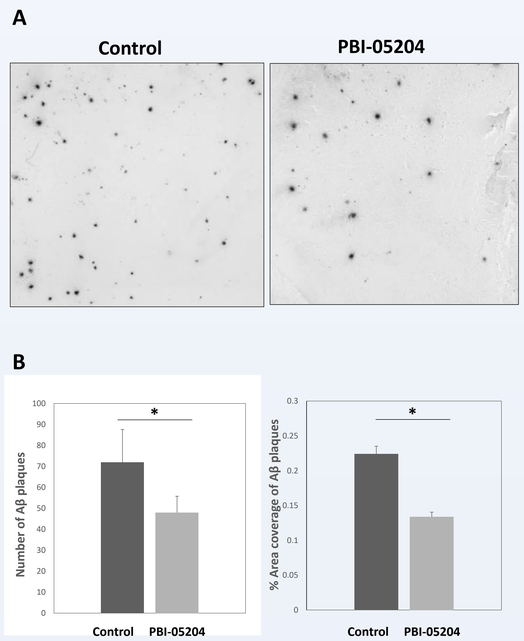


Figure 1. A) Representative images of Aβ plaques in PBI-05204 treated and control groups. Aβ plaques were labelled by the anti-82E1 antibody in cerebral cortex and hippocampus. B) The quantitative analysis of the number of the plaques and percentage area covered by the plaques demonstrates the significant reduction of Aβ plaques in the PBI-05204 treated group. *P<0.05

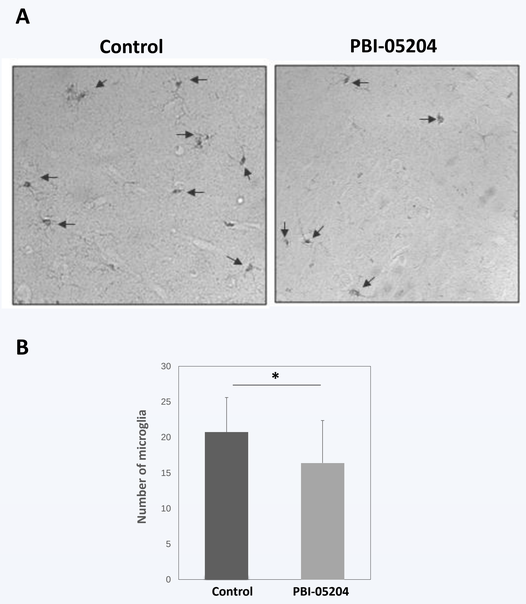


Figure 2. A) Representative images of immunohistochemistry of microglia using anti-Iba1 antibody in hippocampus. B) Quantification of the number of microglial stained by IHC in the treated versus control group. The number of microglia is significantly reduced in the PBI-05204 treated group compared to the control. *p<0.05

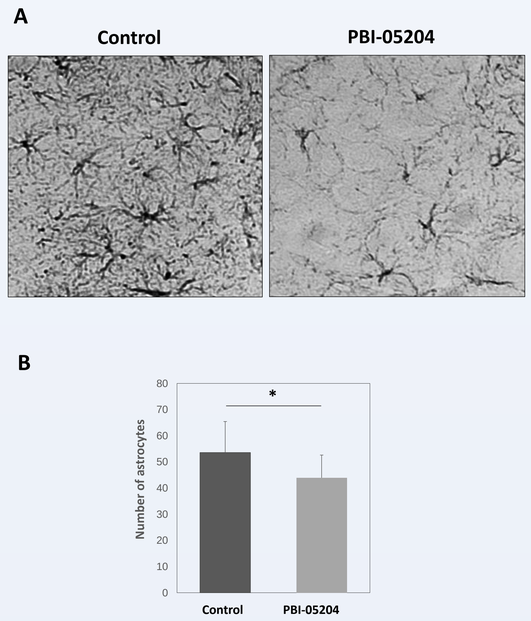


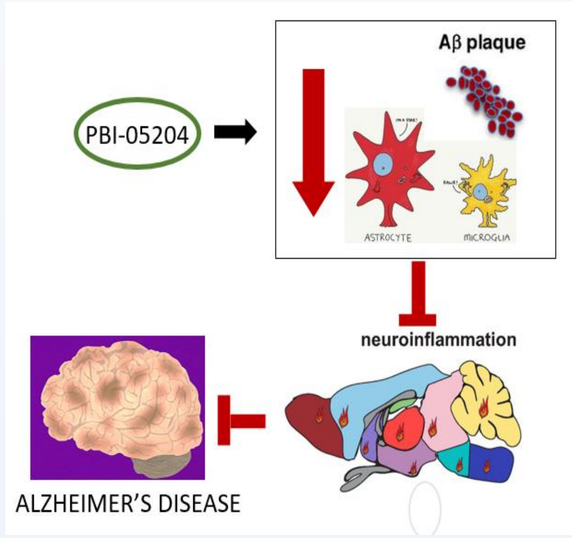
Figure 3. A) Representative images of astrocytes stained by anti-GFAP antibody in PBI-05204 treated versus control hippocampus. B) The number of astrocytes are significantly reduced in the PBI-05204 treated group compared to the control. *P<0.05

CONCLUSION

1.PBI-05204 **significantly reduces Aβ plaque** formation in APP/PSEN1dE9 mice.

2.PBI-05204 **significantly reduces neuroinflammation.**

The significant reduction of the accumulation of Aβ and neuroinflammation by the treatment of PBI-05204 strongly supports the therapeutic potential of PBI-05204 for the treatment of AD.



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