8. Conclusions

The possibility of introducing PM and EJ for the successful management of GLP-1 activity in an attempt to reduce Aβ peptides, tau phosphorylation and neuroinflammation in AD brain warrants further investigation. Evidence suggests that incretins or their analogue liraglutide\textsuperscript{135} and exendin-4\textsuperscript{129} are useful in the treatment of AD. The National Institute of Aging (NIA, USA) is currently recruiting participants for clinical trials on exendin-4. Previous attempts proved the use of sitagliptin, vildagliptin and saxagliptin for the treatment of AD in animal model. However, herbal based DPP-4 inhibitors for the treatment of AD are limited. Our current results on PM and EJ support the use of these herbal DPP-4 inhibitors for the treatment of AD.

The present study demonstrates that an increase in amyloid load, tangles and neuroinflammation cause’s cognitive deficits in STZ induced rat model of AD. PM and EJ exerts complete reversal of cognitive deficits that may be attributed to their effect of lowering amyloid load, tau phosphorylation and neuroinflammation. These results demonstrate that, PM and EJ extracts which are effective in the treatment to T2D, also have neuroprotective properties. However, further investigation is required to elucidate the molecular mechanisms involved in the neuroprotective effects of PM and EJ.

This provide evidence that the neuronal loss in the brain of STZ rat proceeded with the accumulation of plaques and tangles, which was blocked by treatments with PM and EJ. These results suggest that anti-AD-like effects of PM and EJ are related to anti-amyloid property or a yet to be identified mechanism that suppresses the phosphorylation of tau by GLP-1. Nonetheless, we do not exclude the possibility that anti-AD-like effects of PM and EJ are affected by the mechanism that needs to be studied in the future (see the future direction section 9). Because PM and EJ confers beneficial effects on AD-
like brain, it will be of interest to understand the mechanism underlying the action of PM and EJ on the AD-like brain.

9. **Future directions**

Present study demonstrates the use of herbal DPP-4 inhibitors for the treatment of AD. However, several gaps in our understanding of the mechanism behind neuroprotection against STZ induced AD warrants further investigations. Towards that goal, the following points need to be considered:

- Research needs to delineate the kinases and the sites involved in the prevention of tau phosphorylation following PM and EJ treatments.
- The current approach of DPP-4 inhibition using PM and EJ promises to be powerful agents in inhibiting TNF-α and IL-1β in Alzheimer’s affected animals, and future studies will investigate the mechanisms underlying DPP-4 inhibition of neuro-inflammation.
- Investigation is warranted to elucidate other possible neurochemical and molecular mechanisms including glucose-dependent insulinotropic polypeptide involved in the neuroprotective effect of the extracts.
- Investigation on the constituents present in each plant need to be evaluated for their neuroprotective properties in STZ induced AD.