Neuroprotective effects of HM1521, a novel long-acting GLP-1/GIP/Glucagon triple agonist in the neurodegenerative disease models

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ABSTRACT
HM1521 is a novel long-acting GLP-1/GIP/Glucagon triple agonist that is being developed for the treatment of obesity and non-alcoholic fatty liver disease (NAFLD). Accumulated evidences have shown that obesity, type 2 diabetes, and NASD increase the risk of developing progressive neurodegenerative diseases such as Parkinson’s disease (PD) and Alzheimer’s disease (AD). Additionally, both obesity and NASD are the risk factors of the neuroinflammatory process consisting HM1521 have neuroprotective effects in several brain disorders including HM1, AD, and PD.

Previously, we demonstrated that HM1521 exerted neuroprotective effects in MPTP-induced Parkinson’s disease mouse model and the protection of Alzheimer’s disease progression in db/db mice. Chon et al. (2018) reported a reduction of peripheral inflammation by HM1521, which was derived from anti-inflammatory effects by HM1521. Also, HM1521 decreased Aβ1-42 levels in the brain (Chon et al., 2019). These results suggested that HM1521 could improve neurodegenerative disorders by anti-inflammatory effects. Therefore, this study aims to investigate the neuroprotective effects on PD progression by HM1521.

RESULTS

Functional evaluation in chronic PD mice

Figure 1. Motor function testing effects of HM1521
(a) Traction test (b) Pole test (T-total) (c) Rotarod test

Mechanisms of neuroprotection in chronic PD mice

Figure 2. Dopaminergic neuroprotection by HM1521
(a) Dopaminergic neuron staining (TH, tyrosine hydroxylase)

Figure 3. Anti-inflammatory effects of HM1521

Figure 4. Inhibited accumulation of Aβ1-42

Figure 5. Reduced inflammation by HM1521

CONCLUSIONS

In summary, HM1521 reduced locomotor impairment in a chronic PD mouse model, which is shown by reduced DA cell loss, hyperactivation of microglia, and reduced Aβ1-42 levels in the brain. Further studies are required to determine the potential therapeutic effects of HM1521 for PD and Alzheimer’s disease.

REFERENCES

5. Sun SM et al., Diabetes 65(12):3109-316 (2016)