Effect of HM15211, a novel long-acting GLP-1/GIP/Glugon tripeptide agonist in the neurodegenerative disease models

Won Ki Kim¹, Jeong A Kim¹, Sang Yun Kim², Sang-Hyun Lee³, Sung Min Bae¹, In Young Choi¹, Young Hoon Kim¹, ²Hanmi Pharm. Co., Ltd, Seoul, South Korea

ABSTRACT
Metabolic disturbances such as diabetes and obesity, are a potent risk factors for the progressive neurodegenerative diseases such as Parkinson’s disease (PD) and Alzheimer’s disease (AD). Recent evidence suggests that anti-diabetic or anti-obesity drug may be useful for the treatment of neurodegenerative diseases. Recently, we have developed HM15211, a novel long-acting GLP-1/GIP/Glugon tripeptide agonist. Previous studies have revealed that HM15211 achieved neuroprotective effects in the MPTP-induced PD model (2), the protection of AD progression in diabetic model, and neuroprotective effect in the rearing-rearing experimental autoimmune encephalomyelitis (EAE) model of MS. In chronic PD model, HM15211 administration protected dopaminergic neuronal death and decreased alpha synuclein in striatum. Together with a significant reduction in motor impairments in behaviour tests. In addition, HM15211 reversed inflammatory cytokines and antioxidant stress markers in aged ddb mice which have a pathological characters of AD. These results suggest that HM15211 have a protective effect in progression from diabetes to AD. In another experiment, HM15211 have shown the anti-inflammatory and neuroprotective effects in the EAE model mouse of DB Henry. We evaluated the protective effects of HM15211 in EAE model, the mice were subcutaneously treated with HM15211 from day 1 to day 14.

METHODS

- Chronic Parkinson’s disease mice model was induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) in combination with intraperitoneal injection. Injection was performed once a week for 5 weeks and HM15211 was subcutaneously administered once a week for 8 weeks.
- BMs were well-established diabetic model. It has been reported that db mice increase amyloid beta 1-42. Thus we chose db mice to elucidate the protective effect of HM15211 on the development of Alzheimer’s disease. It was observed that db mice智商 increased amyloid beta 1-42. A Traction test model was established by injecting S.c. with an emulsion of PLP191-193 in complete Freund’s adjuvant followed by administration of pertussis toxin was utilized. To evaluate the protective effects of HM15211 on EAE model, the mice were subcutaneously treated with HM15211 from day 1 to day 14.

RESULTS

Figure 2. Dopaminergic neuroprotection by HM15211 (a) Dopaminergic neuron staining (TH, tyrosine hydroxylase)

- Neuroprotective effects of GLP-1, GIP and Glugon
- Neuroprotective effects of GLP-1, GIP and Glugon
- Neuroprotective effects of GLP-1, GIP and Glugon
- Neuroprotective effects of GLP-1, GIP and Glugon

BACKGROUND

- Neuroprotective effects of GLP-1, GIP and Glugon
- Neuroprotective effects of GLP-1, GIP and Glugon
- Neuroprotective effects of GLP-1, GIP and Glugon
- Neuroprotective effects of GLP-1, GIP and Glugon

CONCLUSIONS

- Neuroprotective effects of GLP-1, GIP and Glugon
- Neuroprotective effects of GLP-1, GIP and Glugon
- Neuroprotective effects of GLP-1, GIP and Glugon
- Neuroprotective effects of GLP-1, GIP and Glugon

REFERENCES

2. Rami Abu Farro et al., Am J Physiol Regul Integr Comp Physiol 301 R668-R673 (2011)
3. Yuanyi Li et al., Neuropharmacology 90, 2554-263 (2010)

Neuroprotective effects in chronic PD model

Figure 3. Anti-inflammatory effects of HM15211

- Neuroprotective effects in chronic PD model
- Neuroprotective effects in chronic PD model
- Neuroprotective effects in chronic PD model
- Neuroprotective effects in chronic PD model

Figure 4. Inhibited accumulation of Aβ in EAE mouse model of multiple sclerosis

- Neuroprotective effects in chronic PD model
- Neuroprotective effects in chronic PD model
- Neuroprotective effects in chronic PD model
- Neuroprotective effects in chronic PD model

Figure 5. Reduced inflammation and oxidative stress by HM15211

- Neuroprotective effects in chronic PD model
- Neuroprotective effects in chronic PD model
- Neuroprotective effects in chronic PD model
- Neuroprotective effects in chronic PD model

Figure 6. Prevention effects of HM15211 in EAE mouse model

- Neuroprotective effects in chronic PD model
- Neuroprotective effects in chronic PD model
- Neuroprotective effects in chronic PD model
- Neuroprotective effects in chronic PD model

Neuroprotection of chondrogenic PD model

Figure 2. Dopaminergic neuroprotection by HM15211 (a) Dopaminergic neuron staining (TH, tyrosine hydroxylase)

- Neuroprotection of chondrogenic PD model
- Neuroprotection of chondrogenic PD model
- Neuroprotection of chondrogenic PD model
- Neuroprotection of chondrogenic PD model

Neuroprotection of chondrogenic PD model

Figure 3. Anti-inflammatory effects of HM15211

- Neuroprotection of chondrogenic PD model
- Neuroprotection of chondrogenic PD model
- Neuroprotection of chondrogenic PD model
- Neuroprotection of chondrogenic PD model

Neuroprotection of chondrogenic PD model

Figure 4. Inhibited accumulation of Aβ in EAE mouse model of multiple sclerosis

- Neuroprotection of chondrogenic PD model
- Neuroprotection of chondrogenic PD model
- Neuroprotection of chondrogenic PD model
- Neuroprotection of chondrogenic PD model

Neuroprotection of chondrogenic PD model

Figure 5. Reduced inflammation and oxidative stress by HM15211

- Neuroprotection of chondrogenic PD model
- Neuroprotection of chondrogenic PD model
- Neuroprotection of chondrogenic PD model
- Neuroprotection of chondrogenic PD model

Neuroprotection of chondrogenic PD model

Figure 6. Prevention effects of HM15211 in EAE mouse model

- Neuroprotection of chondrogenic PD model
- Neuroprotection of chondrogenic PD model
- Neuroprotection of chondrogenic PD model
- Neuroprotection of chondrogenic PD model