Effect of a novel long-acting GLP-1/GIP/Glucagon triple agonist (HM15211) in a NASH and fibrosis animal model

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ABSTRACT
NASH (Nonalcoholic Steatohepatitis), a potential consequence of NAFLD, may lead to end stage liver disease including cirrhosis and hepatocellular carcinoma. Despite its severity and prevalence, NASH currently lacks an effective treatment option. HM15211 is a novel long-acting GLP-1/GIP/Glucagon triple agonist, HM15211. Previously, we showed that HM15211 reduces portal resistance in LIRI (lipotoxicity-induced) cirrhotic mice. In this study, we investigated the effects of HM15211 in NASH and fibrosis by using DIO mice and MCD-diet mice.

RESULTS
Liver preferential distribution of HM15211
Figure 1. Time-dependent tissue distribution of HM15211 in SD rats (n=3).

Figure 3. Effect of HM15211 on NASH prognosis markers in MCD-diet mice (n=7).

Figure 5. Effect of HM15211 on hepatic NASH/fibrosis marker gene expression in MCD-diet mice (n=7).

Figure 6. Therapeutic effect of HM15211 on NASH and fibrosis in MCD-diet mice (n=7).

METHODS
To investigate the effects of HM15211 on hepatic lipid metabolism related gene expression, liver tissue samples were prepared after 4 weeks treatment of HM15211 in DIO mice. Then, the qPCR was performed to compare liver-related gene expression (e.g. lipogenic genes SREBP1-C, ACC1, ACC2, PG and ACADVL) and fibrosis-related gene expression (Collagen-1α, TIM1-3, and TGF-β) in the HM15211 treated mice

BACKGROUND
HM15211, long-acting GLP-1/GIP/Glucagon tri-agonist, might have therapeutic potential in NASH by various MoA in liver.

CONCLUSIONS
• HM15211 reduced lipid levels in the liver and serum, reduced inflammation, fibrosis, and also improved insulin resistance in NASH and fibrosis.
• HM15211 shows potential as an effective treatment option for NASH patients.

REFERENCES
• Harries et al. PLoS ONE;2010;5(11), e17948

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