Therapeutic effect of a long-acting GLP-1/GIP/Glucagon triple agonist (HM15211) in a dyslipidemia animal model

Jae Hyuk Choi, Hyo Sang Jo, Jung Kuk Kim, Sang Don Lee, Jong Soo Lee, Sang-Hyun Lee, In Young Choi

Hannmi Pharm. Co., Ltd, Seoul, South Korea

ABSTRACT

Dyslipidemia is a well-established risk factor for cardiovascular disease. Although an efficacy has been demonstrated for several drugs, drawbacks of current medical treatment remain unmet. Recently, therapeutic agents that target the free neutral chain of activation (HM15211) have been reported. As a result, dyslipidemia patients are expected to have several pathways for lipid metabolism, suggesting a potential therapeutic option for dyslipidemia. Here, we investigated the effect of HM15211 on various models of mouse HM

METHODS

To evaluate the therapeutic efficacy in dyslipidemia, high-fat and high-fructose diet hamsters were administrated with HM15211, and lipid profiles were monitored. For efficacy comparison, commercially available dyslipidemia drugs such as evolocumab and rosuvastatin were included. At the end of study, liver tissue samples were prepared, and protein expression of LDLR and HMGCR was thoroughly evaluated.

To evaluate the potential inhibitory effect of HM15211 on lipid absorption, and lipid tolerance test was performed. Slightly overweight-treated normal mice were fed with oil-free, followed by blood TG monitoring.

For an in vitro MTT study, cells (HepG2 cells treated with HM15211 were subjected to western blot analysis (LDLR, and HMGCR) and qPCR (lipid metabolism-related genes).

Lipid lowering efficacy in an animal model

Background

Known targets of current dyslipidemia drugs, and suggested effects of HM15211 on lipid metabolism

Inhibition of lipid absorption by HM15211

HMGCR inhibition by HM15211

Enhanced LDL clearance by HM15211

Improved FFA metabolism by HM15211

Conclusions

In dyslipidemia hamsters, HM15211 provides greater CHD lowering than commercial dyslipidemia drugs such as evolocumab and statin. HM15211 might have several pathways for lipid metabolism, suggesting a potential therapeutic option for dyslipidemia patients.

References


American Diabetes Association's (ADA) 79th Scientific Sessions, San Francisco, CA, USA; June 07-11, 2019