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MEETING ABSTRACT

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12-Monoketocholate: a new perspective in metabolic syndrome treatments

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Background: Recent studies have revealed that bile acids (BAs) are not only facilitators of dietary lipid absorption but also important signaling molecules exerting multiple physiological functions. 12-Monoketocholate (12-MKC) is a stable semisynthetic bile acid salt with low toxicity. It has shown significant hypoglycemic activity in its own and a potential to enhance absorption of various active principles that are used in prevention and treatment of dislipidemia, diabetes mellitus and hypertension. This review summarizes recent analyses of 12-MKC as a potential therapeutic agent and development of novel 12-MKC-based therapeutics for treating disorders in metabolic syndrome.

Methods: The data of 12-MKC effects in metabolic syndrome have been provided from review and original scientific articles, published from 1999 to 2018. The research was performed using the following key words: bile acids, 12-MKC, diabetes, obesity, metabolism.

Results: A study conducted by Mikov *et al.* [1] indicated that after a nasal administration of 12-MKC alone in rats with type 1 diabetes, the glucose concentration was about 36 % less than that obtained after subcutaneous insulin administration. The authors also confirmed that the oral administration of 12-MKC decreases the blood glucose level in diabetic rats. A recent study [2] has shown that the combination of 12-MKC and gliclazide exhibits even a better glycemic control in probiotic pretreated diabetic rats than 12-MKC alone. Overviewing numerous studies about 12-MKC as a potential adjuvant it has been derived that after oral administration in rats, 12-MKC has a promotory effect on the action of gliclazide, lovastatin, stevioside and enhances nasal permeation of insulin.

Discussion: 12-MKC has positive effects in metabolic syndrome, but the mechanisms remain poorly understood. Activation of farnesoid X receptor (FXR) and G protein-coupled bile acid receptor (TGR5) signaling pathways is one of the possible explanations. By activating FXR, BAs supress phosphoenolpyruvate carboxykinase (PEPCK), which is the rate-limiting enzyme of gluconeogenesis. In addition, enzymes such as glucose 6-phosphatase and fructose 1,6-bisphosphatase 1 which also participate in gluconeogenesis are shown to be repressed by BAs. The TGR5 signaling pathway stimulates energy expenditure in both brown adipose tissue as well as skeletal muscle. Suggested mechanisms of permeation enhancement involve 12-MKC effect on the efflux transporters in various tissues and the solubilization effect of this salt. Since 12-MKC is less hydrophobic and has a higher critical micellar concentration (CMC) than other bile salts, toxicity is minimised. Therefore, 12-MKC may serve as a potent therapeutic approach for the treatment of obesity, type 2 diabetes, and other components of the metabolic syndrome in humans.

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