5-Amino-1MQ

Purity: >98% (HPLC on request) I Molecular Formula: C10H11N2 Molecular Weight: 159.21 g/mol I Sequence: Non-Peptide

DESCRIPTION:

5-Amino-1MQ is a small, selective, membrane permeable molecule that is an inhibitor of nicotinamide N-methyltransferase (NNMT), a cytosolic enzyme that plays a role in cellular metabolism and energy homeostasis. NNMT has been found to be up-regualted in white adipose tissue of mice compared to other tissues, thus, NNMT is an ideal target for anti-obesity medication. 5-Amino-1MQ is a derivative of methylquinolinium (MQ) which has exhibited a high efficacy in NNMT inhibition, cell viability, and membrane permeability. It did not have any effect on the activity of any other enzymes in the relevant metabolic cycles, therefore reducing the risks of potential side effects. This NNMT inhibitor could be used to prevent adipogenesis and type II diabetes and reverse diet-induced obesity as a result of increased intracellular NAD+ and SAM.

In a study using diet-induced obsese mice fed a high fat diet, the effects of 5-Amino-1MQ on obesity measures and plasma lipid were evaluated. After 11 days, mice treated with 5-Amino-1MQ lost weight, exhibited a decrease in white adipose mass and cholesterol levels, and displayed reduced lipogenesis. The results of this study validate NNMT as a practical target to treat obesity and related metabolic conditions and support the development of an NNMT inhibitor therapeutics to reverse diet-induced obesity.

PROTOCOL:

Content & Potency: 50mg capsule provided in a quantity of 90 capsules
Suggested dosage: Take 3 capsules daily

CLINICAL RESEARCH:

Selective and membrane-permeable small molecule inhibitors of nicotinamide N-methyltransferase reverse high fat diet-induced obesity in mice

There is a critical need for new mechanism-of-action drugs that reduce the burden of obesity and associated chronic metabolic comorbidities. A potentially novel target to treat obesity and type 2 diabetes is nicotinamide-N-methyltransferase (NNMT), a cytosolic enzyme with newly identified roles in cellular metabolism and energy homeostasis. To validate NNMT as an anti-obesity drug target, we investigated the permeability, selectiv¬ity, mechanistic, and physiological properties of a series of small molecule NNMT inhibitors. Membrane permeability of NNMT inhibitors was characterized using parallel artificial membrane permeability and Caco-2 cell assays. Selectivity was tested against structurally-related methyltransferases and nicotinamide adenine dinucleotide (NAD+) salvage pathway enzymes. Effects of NNMT inhibitors on lipogenesis and intracellular levels of metabolites, including NNMT reaction product 1-methylnicotinamide (1-MNA) were evaluated in cultured adipocytes. Effects of a potent NNMT inhibitor on obesity measures and plasma lipid were assessed in diet-induced obese mice fed a high-fat diet. Methylquinolinium scaffolds with primary amine substitutions displayed high permeability from passive and active transport across membranes. Importantly, methylquinolinium analogues displayed high selectivity, not inhibiting related SAM-dependent methyltransferases or enzymes in the NAD+ salvage pathway. NNMT inhibitors reduced intracellular 1-MNA, increased intracellular NAD+ and S-(5'-adenosyl)-L-methionine (SAM), and suppressed lipogenesis in adipocytes. Treatment of diet-induced obese mice systemically with a potent NNMT inhibitor significantly reduced body weight and white adipose mass, decreased adipocyte size, and lowered plasma total cholesterol levels. Notably, administration of NNMT inhibitors did not
impact total food intake nor produce any observable

adverse effects. These results support development of small molecule NNMT inhibitors as therapeutics to reverse diet-induced obesity and validate NNMT as a viable target to treat obesity and related metabolic conditions. Increased flux of key cellular energy regulators, including NAD+ and SAM, may potentially define the therapeutic mechanism-of-action of NNMT inhibitors.

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