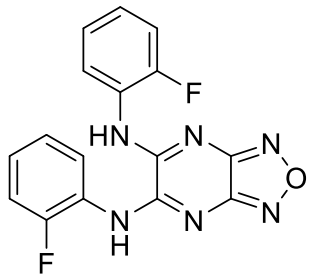
Product data sheet

MedKoo Cat#: 522443 Name: BAM15 CAS#: 210302-17-3 Chemical Formula: $C_{16}H_{10}F_2N_6O$ Exact Mass: 340.08842 Molecular Weight: 340.29	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
BAM15 is a potent and selective mitochondrial uncoupler or protonophore. Chemical mitochondrial uncouplers are lipophilic weak acids that transport protons into the mitochondrial matrix via a pathway that is independent of ATP synthase, thereby uncoupling nutrient oxidation from ATP production. These uncouplers have potential for the treatment of diseases such as obesity, Parkinson's disease, and aging.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	20	58.8

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.94 mL	14.69 mL	29.39 mL
5 mM	0.59 mL	2.94 mL	5.88 mL
10 mM	0.29 mL	1.47 mL	2.94 mL
50 mM	0.06 mL	0.29 mL	0.59 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Kenwood BM, Weaver JL, Bajwa A, Poon IK, Byrne FL, Murrow BA, Calderone JA, Huang L, Divakaruni AS, Tomsig JL, Okabe K, Lo RH, Cameron Coleman G, Columbus L, Yan Z, Saucerman JJ, Smith JS, Holmes JW, Lynch KR, Ravichandran KS, Uchiyama S, Santos WL, Rogers GW, Okusa MD, Bayliss DA, Hoehn KL. Identification of a novel mitochondrial uncoupler that does not depolarize the plasma membrane. Mol Metab. 2013 Nov 28;3(2):114-23. doi: 10.1016/j.molmet.2013.11.005. PMID: 24634817; PMCID: PMC3953706.

2. Axelrod CL, King WT, Davuluri G, Noland RC, Hall J, Hull M, Dantas WS, Zunica ER, Alexopoulos SJ, Hoehn KL, Langohr I, Stadler K, Doyle H, Schmidt E, Nieuwoudt S, Fitzgerald K, Pergola K, Fujioka H, Mey JT, Fealy C, Mulya A, Beyl R, Hoppel CL, Kirwan JP. BAM15-mediated mitochondrial uncoupling protects against obesity and improves glycemic control. EMBO Mol Med. 2020 Jul 7;12(7):e12088. doi: 10.15252/emmm.202012088. Epub 2020 Jun 10. PMID: 32519812; PMCID: PMC7338798.

In vivo study

1. Kenwood BM, Weaver JL, Bajwa A, Poon IK, Byrne FL, Murrow BA, Calderone JA, Huang L, Divakaruni AS, Tomsig JL, Okabe K, Lo RH, Cameron Coleman G, Columbus L, Yan Z, Saucerman JJ, Smith JS, Holmes JW, Lynch KR, Ravichandran KS, Uchiyama S, Santos WL, Rogers GW, Okusa MD, Bayliss DA, Hoehn KL. Identification of a novel mitochondrial uncoupler that does not

depolarize the plasma membrane. Mol Metab. 2013 Nov 28;3(2):114-23. doi: 10.1016/j.molmet.2013.11.005. PMID: 24634817; PMCID: PMC3953706.

2. Axelrod CL, King WT, Davuluri G, Noland RC, Hall J, Hull M, Dantas WS, Zunica ER, Alexopoulos SJ, Hoehn KL, Langohr I, Stadler K, Doyle H, Schmidt E, Nieuwoudt S, Fitzgerald K, Pergola K, Fujioka H, Mey JT, Fealy C, Mulya A, Beyl R, Hoppel CL, Kirwan JP. BAM15-mediated mitochondrial uncoupling protects against obesity and improves glycemic control. EMBO Mol Med. 2020 Jul 7;12(7):e12088. doi: 10.15252/emmm.202012088. Epub 2020 Jun 10. PMID: 32519812; PMCID: PMC7338798.

7. Bioactivity

Biological target:

BAM 15 is a mitochondrial protonophore uncoupler and an oxidative phosphorylation (OXPHOS) uncoupler.

In vitro activity

The effects of BAM15 was measured versus FCCP on plasma membrane electrophysiology using whole cell voltage and current clamp recordings. As expected, under voltage clamp conditions at a holding potential of −70 mV, FCCP induced an inward current that was dose-dependent and associated with an increase in conductance (Figure 4A–F). In contrast, BAM15 elicited no appreciable change in current in the same cells. Under current clamp conditions, FCCP caused reversible and repeatable plasma membrane depolarization, whereas BAM15 had no effect (Figure 4G and H). The differential effects of BAM15 and FCCP on plasma membrane properties were independent of the order of uncoupler application (not shown). Furthermore, BAM15-treated cells were more viable than FCCP-treated cells when administered across a broad dosing range up to 50 μM (Suppl. Figure 6). These data indicate that BAM15 does not share the adverse plasma membrane effects that may contribute to cytotoxicity.

Reference: Mol Metab. 2013 Nov 28;3(2):114-23. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/24634817/

In vivo activity

To determine the efficacy and feasibility of BAM15 in vivo, 10‐week‐old male diet‐induced obese (DIO) C57BL/6J mice were randomized to 3 weeks of CTRL (60% HFD) or BAM15 (60% HFD + 0.1% w/w BAM15). Ad libitum consumption of BAM15 resulted in consumption of ~85 mg/kg/day (Fig EV2A), with peak serum concentrations of ~5 μM and a half‐life of ~3 h (Fig 4A). Further assessment revealed primary distribution into adipose tissue depots and to lesser extent, liver, heart, and kidneys (Figs 4B and EV2B). By day 9, BAM15 animals displayed reduced body weight relative to control (Figs 4C and EV2C, and EV3A), an effect that persisted throughout the remainder of the treatment period. BAM15 did not affect daily (Fig EV2D and E) or cumulative food intake until day 20 (Fig 4D), at which point a mean difference in body weight of 7.5 g was observed. Neither acute intraperitoneal injection (Fig 4E) of BAM15 nor chronic oral administration (Figs 4F and EV2F) altered body temperature. Furthermore, acute oral administration of BAM15 did not alter tail heat dissipation (Fig EV2G and H). Unlike CTRL, which gained both fat and lean mass during the treatment period, BAM15 animals displayed reduced fat mass with no change in lean mass compared with baseline (Fig 4G and H). The reductions in fat mass were consistent with marked reductions in gonadal white adipose tissue (gWAT), inguinal WAT (iWAT), retroperitoneal WAT (rpWAT), and brown adipose tissue (BAT) depot weights (Fig EV3). However, there were no differences in muscle depots, such as the mixed gastrocnemius or heart (Fig EV3). In addition to adipose depots, liver weight was reduced in BAM15‐treated animals (Fig EV3), along with fasting plasma glucose and insulin (Fig 4I and J). Given the reductions in fasting glucose and insulin, glycemic control was then assessed by intraperitoneal glucose tolerance testing (IPGTT). It was observed that glucose clearance was improved in BAM15 animals relative to CTRL (Figs 4K and L and EV2I). To determine whether alterations in energy expenditure explained the reductions in body weight and adiposity, animals were placed in a metabolic chamber and examined over a 7‐day period. Oxygen consumption and total daily energy expenditure were increased (Fig 4M and N), whereas the respiratory exchange ratio (RER) was decreased (Fig 4O) in BAM15‐treated animals. Notably, the daily effect on energy expenditure was driven by changes in dark phase expenditure and consumption. In addition to energy expenditure, BAM15 preserved locomotor function, which decreased from baseline in CTRL animals (Fig EV2J and K). Cumulative water consumption was unaffected by BAM15 (Fig EV2L). To confirm that the improvements in weight regulation were attributable to increased energy expenditure, fecal lipid content was measured and no differences between groups was observed (Fig 4P). Taken together, these data suggest that BAM15 protects against diet‐induced obesity and improves glycemic control by increasing energy expenditure and reducing adiposity.

Reference: EMBO Mol Med. 2020 Jul 7;12(7):e12088. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/32519812/

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