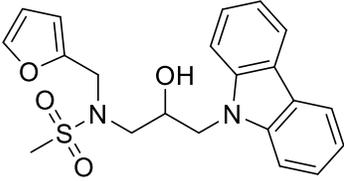


# Product data sheet



MedKoo Cat#: 522570 Name: KL001 CAS#: 309928-48-1 Chemical Formula: C <sub>21</sub> H <sub>22</sub> N <sub>2</sub> O <sub>4</sub> S Exact Mass: 398.13 Molecular Weight: 398.47	
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:

KL001 is a Cryptochrome protein (CRY) stabilizer. KL001 prevented ubiquitin-dependent degradation of CRY, resulting in lengthening of the circadian period. In combination with mathematical modeling, our studies using KL001 revealed that CRY1 and CRY2 share a similar functional role in the period regulation. Furthermore, KL001-mediated CRY stabilization inhibited glucagon-induced gluconeogenesis in primary hepatocytes. KL001 thus provides a tool to study the regulation of CRY-dependent physiology and aid development of clock-based therapeutics of diabetes.

## 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	32.46	81.47

## 4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.51 mL	12.55 mL	25.10 mL
5 mM	0.50 mL	2.51 mL	5.02 mL
10 mM	0.25 mL	1.25 mL	2.51 mL
50 mM	0.05 mL	0.25 mL	0.50 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

- Chang J, Garva R, Pickard A, Yeung CC, Mallikarjun V, Swift J, Holmes DF, Calverley B, Lu Y, Adamson A, Raymond-Hayling H, Jensen O, Shearer T, Meng QJ, Kadler KE. Circadian control of the secretory pathway maintains collagen homeostasis. *Nat Cell Biol.* 2020 Jan;22(1):74-86. doi: 10.1038/s41556-019-0441-z. Epub 2020 Jan 6. PMID: 31907414.
- Hirota T, Lee JW, St John PC, Sawa M, Iwaisako K, Noguchi T, Pongsawakul PY, Sonntag T, Welsh DK, Brenner DA, Doyle FJ 3rd, Schultz PG, Kay SA. Identification of small molecule activators of cryptochrome. *Science.* 2012 Aug 31;337(6098):1094-7. doi: 10.1126/science.1223710. Epub 2012 Jul 12. PMID: 22798407; PMCID: PMC3589997.

### In vivo study

- Solovev IA, Shaposhnikov MV, Moskalev AA. Chronobiotics KL001 and KS15 Extend Lifespan and Modify Circadian Rhythms of *Drosophila melanogaster*. *Clocks Sleep.* 2021 Aug 20;3(3):429-441. doi: 10.3390/clockssleep3030030. PMID: 34449576; PMCID: PMC8395451.
- Iida M, Nakane Y, Yoshimura T, Hirota T. Effects of Cryptochrome-modulating compounds on circadian behavioral rhythms in zebrafish. *J Biochem.* 2021 Sep 16;mvab096. doi: 10.1093/jb/mvab096. Epub ahead of print. Erratum in: *J Biochem.* 2022 Feb 18;: PMID: 34528676.

# Product data sheet



## 7. Bioactivity

### Biological target:

KL001 is a first-in-class cryptochrome stabilizer which specifically interacts with CRY1 and CRY2 and prevents ubiquitin-dependent degradation of CRY, resulting in lengthening of the circadian period.

### In vitro activity

KL001 at 2.5  $\mu\text{M}$  and 10  $\mu\text{M}$  was well tolerated by tendon fibroblasts but led to arrhythmic bioluminescence in PER2::LUC tendon fibroblasts. The addition of KL001 to control tendon fibroblasts led to increased steady-state levels of Sec61a2, Mia3, Pde4d and Vps33b transcripts as well as increased numbers of collagen fibres per cell. Conversely, KL001 did not restore rhythmic bioluminescence to PER2::LUC::Clock $\Delta$ 19 fibroblasts, and the addition of KL001 to Clock $\Delta$ 19 fibroblasts resulted in decreased levels of Mia3, Serpinh1, Pde4d and Vps33b as well as a decrease in the number of collagen fibres per cell in these cells. The increase in collagen fibre numbers in wild-type cells treated with KL001 (which became arrhythmic) and the decrease in collagen fibre numbers in Clock $\Delta$ 19 cells treated with KL001 indicates that rhythmicity in the secretory pathway is required for collagen fibre homeostasis.

Reference: Nat Cell Biol. 2020 Jan;22(1):74-86. <https://pubmed.ncbi.nlm.nih.gov/31907414/>

### In vivo activity

Statistically significant results of the assessment of differences in indicators in groups receiving activator KL001 at different concentrations indicate the ability of KL001 to prolong the lifespan of Drosophila. Therefore, for a concentration of 5  $\mu\text{M}$ , an increase of 3.5% is shown for the average lifespan,  $p < 0.00001$ , according to the  $\chi^2$ -test), 2% for median lifespan (50% of population mortality),  $p < 0.001$ , in accordance to the Gehan-Breslow-Wilcoxon test. The age of 90% mortality of the population that received 5 $\mu\text{M}$  KL001 with food increased by 14%,  $p < 0.05$ , is in accordance to the Wang-Allison test. The time of 90% mortality of the population was subjected to a statistically significant effect of KL001 in all variants of the experiment; there was an increase in the indicator by 9–14%,  $p < 0.05$ , according to the Wang-Allison test. This phenomenon may suggest the presence of the mechanism associated with improvement of fat body glucose deposits' utilization in starvation conditions which is activated by dCRY binding KL001.

Reference: Clocks Sleep. 2021 Aug 20;3(3):429-441. <https://pubmed.ncbi.nlm.nih.gov/34449576/>

*Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.*