Product Data Sheet

Product Name: Solutol HS-15
Cat. No.: GC30012

Chemical Properties

Cas. No.	61909-81-7		
SMILES	CCCCCCC(O)CCCCCCCCCCC(OCCO)=O.[n]		
Formula	$(C_2H_4O)nC_{18}H_{36}O_3$	M.Wt	
Solubility	Water : 25 mg/mL	Storage	Store at 4°C, sealed storage, away from moisture
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	Solutol HS-15		

Protocol

Cell experiment [1]:

Cell lines	Rat hepatocytes
Preparation Method	Hepatocytes were isolated from the in situ perfusion of a whole liver from male Wistar rats. The uptake of colchicine into the cells was determined using a centrifugal filtration technique through a silicone oil layer. These samples were incubated either in the presence or in the absence of Solutol HS 15 at different concentrations (0.0003, 0.003, and 0.03%, w/v)
Reaction Conditions	0.0003, 0.003, and 0.03%, w/v

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Applications	Solutol HS-15 did not impact the uptake of colchicine. At a Solutol HS 15 concentration above its CMC (0.03%, w/v), the amount of colchicine taken up into the cells as well as its uptake velocity were significantly decreased. At 4 °C, a temperature at which active transport processes should be significantly slowed down, Solutol HS 15 at 0.03% did not affect colchicine uptake and/or its association with the cells.

Animal experiment [2]:

Animal models	Rat (MCAO and ACA models of ischemia)
Preparation Method	Solutol HS 15 and dimethyl sulfoxide were dissolved in sterile saline (0.9 % NaCl). 600ml microliters of Solutol HS 15 was heated to 37 °C and dissolved in 1.4 mL of sterile saline to achieve 2 ml/kg injected (IV bolus or IP, daily for 14 days) into the rat used in MCAO and ACA models of ischemia. Adult male Sprague–Dawley rats (250–350 g) were fasted overnight before surgery. The femoral vein and artery were cannulated using a single-lumen (PE-50) catheter for blood pressure monitoring, blood gas analysis, and intravenous (IV) injection of pharmacological agents.
Dosage form	2 ml/kg IV bolus or IP, daily for 14 days

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Applications	Solutol HS-15 (2 ml/kg, IP) was injected chronically for 14 days (once daily). For focal ischemia experiments, Solutol HS-15 was administered following reperfusion after 2 h of middle cerebral artery occlusion (MCAO). Following ACA, the number of surviving hippocampal neurons was enhanced by Solutol-treated HS15 (68 %) rats as compared to ACA only-treated groups. Infarct volume was decreased by Solutol HS-15 (78 %) as compared to saline (vehicle) in MCAO-treated animals. Solutol HS-15 provide robust neuroprotection in both paradigms of ischemia.

References:

[1]. GonzÁlez R C B, Boess F, Durr E, et al. In vitro investigation on the impact of Solutol HS 15 on the uptake of colchicine into rat hepatocytes[J]. International journal of pharmaceutics, 2004, 279(1-2): 27-31.
[2]. Lin H W, Saul I, Gresia V L, et al. Fatty acid methyl esters and Solutol HS 15 confer neuroprotection after focal and global cerebral ischemia[J]. Translational stroke research, 2014, 5(1): 109-117.

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Background

Solutol HS-15 , a clinically approved excipient, has neuroprotective properties[1,2]. Solutol HS 15 (polyoxyethylene esters of 12-hydroxystearic acid) is non-ionic surfactant, with low toxicity in vivo, was shown to reverse completely the multidrug resistance of KB 8-5 and KB 8-5-11 human epidermoid carcinoma cells in vitro but did not potentiate drug toxicity in drug-sensitive KB 3-1 cells[3]. Solutol HS-15 also acts as a permeability enhancer[4].

Solutol HS 15 produced a 35-, 28-, and 42-fold reduction in the resistance of KB 8-5-11 cells to colchicine, vinblastine, and doxorubicin, respectively,at a concentration of 10%

of its own IC_{50} (mean concentration of drug that causes 50% inhibition of cell growth compared to controls). Like verapamil, Solutol HS 15 promoted a 50-fold accumulation of rhodamine 123 in KB 8-5-11 cells, as measured by flow cytometry. Also, Solutol HS 15 and verapamil reduced the efflux of rhodamine 123 from KB 8-5-11 cells previously loaded with rhodamine 123 to a similar low rate. Solutol HS 15 did not affect the transport of alanine or glucose into KB 8-5-11 cells, indicating that its effect upon membrane active transport is not entirely nonspecific.

Solutol HS 15 is a third generation surfactant carrier used to improve the solubility and bioavailability [5,6]. Solutol HS 15 was the most effective to increase the solubility of Pioglitazone HCl by approximately 33 fold whereas Cremophor RH 40 increased approximately 27 folds. Suitability of Solutol HS 15 has earlier been demonstrated with its physiological compatibility and safety [7].There was simultaneous increase in concentration of micelles along with increase in concentration of Solutol HS 15, because the concentration of Solutol HS 15 used in this study was higher than its critical micelle concentration [8]. This study revealed that Solutol HS 15 is an effective carrier in enhancing solubility and stability of the Pioglitazone HCl. [9]

Solutol HS 15 merits consideration as a potential therapeutic agent because of its effectiveness for reversing multidrug resistance in vitro and its low toxicity in vivo. With proper timing and dosage, administration of Solutol HS-15 can be an effective therapy against cerebral ischemia. Following ACA, the number of surviving hippocampal neurons was enhanced by Solutol-treated HS15 (68 %) rats as compared to ACA only-treated groups. Infarct volume was decreased by Solutol HS-15 (78 %) as compared to saline (vehicle) in MCAO-treated animals. Solutol HS-15 provide robust neuroprotection in both paradigms of ischemia. This may prove therapeutically beneficial since Solutol HS-15 is already administered as a solublizing agent to patients.

References:
[1]. Lin H W, Saul I, Gresia V L, et al. Fatty acid methyl esters and Solutol HS 15 confer neuroprotection after focal and global cerebral ischemia[J]. Translational stroke research, 2014, 5(1): 109-117.
[2]. Ku S, Velagaleti R. Solutol HS-15 as a novel excipient[J]. 2010.
[3]. Coon J S, Knudson W, Clodfelter K, et al. Solutol HS 15, nontoxic polyoxyethylene esters of 12-hydroxystearic acid, reverses multidrug resistance[J]. Cancer research,

1991, 51(3): 897-902.
[4]. Shubber S, et al. Mechanism of mucosal permeability enhancement of CriticalSorb? (Solutol? HS15) investigated in vitro in cell cultures. Pharm Res. 2015 Feb;32(2):516-27.
[5].Shamma RN, Basha M. Soluplus: A novel polymeric solubilizer for optimization of Carvedilol solid dispersions: Formulation design and effect of method of preparation. Powder Technol 2013;237:406-14.
[6].Song CK, Yoon IS, Kim DD. Poloxamer-based solid dispersions for oral delivery of docetaxel: Differential effects of F68 and P85 on oral docetaxel bioavailability. Int J Pharm 2016;507(1-2):102-8.
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[9]. Swain R P, Subudhi B B, Ramesh P. Effect of Solutol HS 15 in Solid Dispersions of Pioglitazone Hydrochloride: in vitro and in vivo Evaluation[J]. Indian Journal of Pharmaceutical Sciences, 2019, 81(2): 317-325.

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