Tanshinone IIA sulfonate (sodium) is a water-soluble derivative of tanshinone IIA, which acts as an inhibitor of store-operated Ca\(^{2+}\) entry (SOCE), and is used to treat cardiovascular disorders.

**In Vitro:** Sodium Tanshinone IIA sulfonate (12.5 μM) inhibits hypoxia-induced PKG and PPAR-γ downregulation in PASMCs and distal pulmonary arteries of rats. The suppressive effects of Sodium Tanshinone IIA sulfonate on TRPC1 and TRPC6 expression in hypoxic PASMCs can be prevented by specific knockdown PKG or PPAR-γ. The suppressive effects of Sodium Tanshinone IIA sulfonate on basal calcium concentration and SOCE in hypoxic PASMCs can be reversed by specific knockdown of PKG or PPAR-γ. PKG-PPAR-γ signaling axis participates in the suppressive effects of Sodium Tanshinone IIA sulfonate on proliferation in hypoxic PASMCs. PPAR-γ agonist promotes the protective role of Sodium Tanshinone IIA sulfonate on basal [Ca\(^{2+}\)]\(_i\) and SOCE in hypoxic PASMCs\(^\text{[2]}\). Sodium tanshinone IIA sulfonate inhibits the activity of CYP3A4 in a dose-dependent manner by the HLMs and CYP3A4 isoform. The K\(\text{M}\) and V\(\text{max}\) values of STS are 54.8±14.6 μM and 0.9±0.1 nmol/mg protein/min, respectively, for the HLMs and 7.5±1.4 μM and 6.8±0.3 nmol/nmol P450/min, respectively, for CYP3A4. CYP1A2, CYP2A6, CYP2C9, CYP2D6, CYP2E1, and CYP2C19 show minimal or no effects on the metabolism of STS\(^\text{[3]}\). Sodium Tanshinone IIA sulfonate inhibits the activity of CYP3A4 in a dose-dependent manner in the HLMs and CYP3A4 isoform. Sodium Tanshinone IIA sulfonate primarily inhibits the activities of CYP3A4 in vitro, and Sodium Tanshinone IIA sulfonate has the potential to perpetrate drug-drug interactions with other CYP3A4 substrates\(^\text{[4]}\).

**In Vivo:** Sodium Tanshinone IIA sulfonate (10 mg/kg, 20 mg/kg) and Donepezil shorten escape latency, increase crossing times of the original position of the platform, and increase the time spent in the target quadrant. Sodium Tanshinone IIA sulfonate decreases the activity of acetylcholinesterase (AChE) and increases the activity of choline acetyltransferase (ChAT) in the hippocampus and cortex of SCOP-treated mice. Sodium Tanshinone IIA sulfonate increases the activity of superoxide dismutase (SOD) and decreases the levels of malondialdehyde (MDA) and reactive oxygen species (ROS) in hippocampus and cortex\(^\text{[1]}\). Sodium Tanshinone IIA sulfonate prevention (30 mg/kg/day) alleviates hypoxia-induced characteristic changes in chronic hypoxia PH rat model\(^\text{[2]}\). Sodium Tanshinone IIA sulfonate (20, 10, and 5 mg/kg, i.p.) effectively prevents peritoneal adhesion without affecting anastomotic healing in the rats. Compared with the adhesion model group, the Sodium Tanshinone IIA sulfonate-treated groups show increased peritoneal lavage fluid tPA activity and tPA/PAI-1 ratio in the ischemic tissues with loared TGF-β1 and collagen I expressions in the ischemic tissues\(^\text{[5]}\).

**PROTOCOL (Extracted from published papers and Only for reference)**

**Animal Administration:** Tanshinone IIA sulfonate (sodium) is formulated in CON, 0.9% saline for mice administration\(^\text{[1]}\). Male Kunming mice (KM, weighing 35-40 g) are maintained on standard laboratory conditions with free access to water and food. Mice are randomly divided into five groups: vehicle control group (CON, 0.9% saline, n=10), scopolamine group (SCOP, n=10), low dose Sodium Tanshinone IIA sulfonate group (Sodium Tanshinone IIA sulfonate L, SCOP 3 mg/kg + Sodium Tanshinone IIA sulfonate 10 mg/kg, n=10), high dose Sodium Tanshinone IIA sulfonate group (Sodium Tanshinone IIA sulfonate H, SCOP 3 mg/kg + Sodium Tanshinone IIA sulfonate 20 mg/kg, n=10), and Donepezil group (DON, SCOP 3 mg/kg + ARI 3 mg/kg, n=10). Mice are treated with
saline, Sodium Tanshinone IIA sulfonate, and Donepezil, respectively, by gavage, once per day for two weeks. SCOP is injected from the eighth day for one week (intraperitoneally, IP). The SCOP is injected 0.5 h before the Morris water maze test.

Male Sprague-Dawley rats (200-250 g) are randomly divided into four groups by the random number table: 1) normoxia control group, 2) normoxia + Sodium Tanshinone IIA sulfonate group, 3) hypoxia control group, and 4) hypoxia + Sodium Tanshinone IIA sulfonate group. Groups 1 and 2 are placed in normoxic condition and groups 3 and 4 in a hypoxic cabin with normal pressure, as previously reported, where the oxygen concentration is maintained at 10±1%, in a sustained hypoxic condition for 21 days. Groups 2 and 4, starting from the first day of hypoxia, are, respectively, intraperitoneally injected with 30 mg/kg tanshinone IIA sulfonate; meanwhile, groups 1 and 3 receive the same dose of saline.

References: