**BIOLOGICAL ACTIVITY:**

Imisopasem manganese (M40403) is a stable non–peptidyl mimetic of manganese superoxide MnSOD.

*In Vitro:* M40403 is a small molecule, synthetic manganese containing superoxide dismutase mimetic (SODm) that removes superoxide anions without interfering with other reactive species known to be involved in inflammatory responses (e.g. nitric oxide, NO and peroxynitrite, ONOO–)\(^1\).

*In Vivo:* M40403 is a small–molecule superoxide dismutase mimetic that has shown efficacy in animal model disease states in which superoxide anions are thought to play a key role. M40403 inhibits the inflammatory response following the intrapleural injection of carrageenan in rats. All parameters of inflammation are attenuated by M40403 except for NOx, PGE2 and IL–10 which remains unaltered\(^1\). Decreased apoptosis of the large and particularly the small bowel and marked recovery of both lymphoid and hematopoietic tissues occurs in the M40403 pre–treated mice. M40403 is effective in reducing TBI–induced tissue destruction and has potential as a new radioprotective agent\(^2\).

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

**Animal Administration:**\(^{[1][2]}\)Rat: Male Sprague–Dawley rats are used in the study. M40403 (5-20 mg kg\(^{-1}\)), or an equivalent volume (0.3 mL) of vehicle (26 mm sodium bicarbonate buffer, pH 8.1–8.3), is injected intraperitoneally (i.p.) 15 min before carrageenan. At 4 h after the injection of carrageenan, the animals are killed by inhalation of CO\(_2\)\(^{[1]}\).

Mouse: 30 mg dry powder M40403 is dissolved in 6.0 ml SBC adjusted to pH 8.3 with 1 M NaOH. This stock solution is diluted to 1.25 mg/mL in SBC. Two experimental models are tested. In one, the dose of IR is held constant at 8.5 Gy total body irradiation (TBI). The mice are injected i.p. with a single dose of 40 mg/kg, 30 mg/kg, 20 mg/kg or 10 mg/kg M40403. Thirty minutes later the mice receives 8.5 Gy total body irradiation (TBI). Control animals receives 0.1 ml of SBC buffer prior to TBI. In the other model, groups of 20 mice receives either 6.5 or 7.5 Gy TBI. One half of each group is treated with 2.0 mg/kg M40403 i.p. and the other with SBC 30 min before TBI. All are followed for survival\(^{[2]}\).

**References:**

