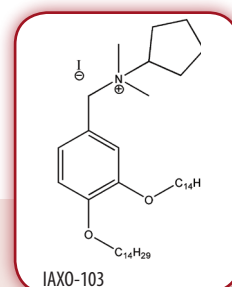


PRODUCT DATA SHEET

IAXO-103 (CD14/TLR4 Antagonist) (synthetic)

Cat. No.: IAX-600-003

Date: 10-Aug-2015



NAME:	N-(3,4-Bis-tetradecyloxy-benzyl)-N-cyclopentyl-N,N-dimethylammonium iodide.
SYNONYMS:	Small molecule CD14/TLR4 ligand/modulator. Benzylammonium lipid. Lipid A analogue.
FORMULA:	C ₄₂ H ₇₈ INO ₂ .
MW:	755.98 g/mol (iodide salt).
CAS NUMBER:	1202208-36-3.
PURITY:	≥98% according to TLC, NMR, MS analysis.
APPEARANCE:	White solid.
SOLUBILITY:	Soluble in Methanol, DMSO and Ethanol 1:1 (vol : vol): >10mM.
HANDLING:	Reconstitution: For a 2mM stock solution, dissolve total vial content in 661µl (1 mg size) or 3,306µl (5mg size) in (1:1) DMSO/Ethanol (vol:vol).
ACTIVITY:	Described to interfere with human, rat and mouse TLR4/CD14 signaling, other species not tested. Optimal working concentration depends upon the type, purity and concentration and of TLR4 ligand, carrier protein such as LPS-binding protein (LBP), soluble and membrane-bound CD14, the presence of TLR4 co-receptors (e.g. CD36) as well on type and time of read-out (e.g. cytokine measurement in cell culture supernatant) or the biological outcome of <i>in vivo</i> experiments and therefore needs to be determined for each application. Recommended starting concentration: <i>in vitro</i> : 5µM, <i>in vivo</i> (rodent): 3mg/kg. Recommended compound: IAXO-202 (Cat. No.: IAX-600-005).
SHIPPING:	Ambient.
STORAGE:	4°C.
STABILITY:	12 months after receipt as supplied.

General Information:

Persistent inflammation has been implicated in the pathogenesis not only of diverse chronic diseases such as neuropathic pain, atherosclerosis, chronic hepatitis, and abdominal aortic aneurysm, but also acute organ failure, cardiac infarct and stroke. The Toll-like receptor (TLR) family members are key contributors to these pro-inflammatory conditions. These pattern recognition receptors respond to molecular patterns in components of bacteria and viruses. In addition to their role in detecting pathogen associated molecular patterns (PAMPs), TLRs can also sense endogenous danger (or tissue damage) associated molecular patterns (DAMPs) and have been implicated in perpetuating inflammatory cascades in the absence of invading microbes or other pathogens. TLR4's well-known key role in orchestrating innate and adaptive immune response to Gram-negative bacteria now extends into the area of mediating auto-inflammation and tissue repair and remodelling.

The novel IAXO classes of glycolipid and benzylammonium lipids are synthetic TLR4/CD14 ligands with TLR4 modulating activities *in vitro*, and conferring protection against TLR4/CD14-mediated tissue damage and inflammation *in vivo* [1-6]. As research tools IAXOs are useful to explore CD14-dependent and TLR4-independent pathways and TLR4 activation by endogenous ligands (e.g. hyaluronic acid oligosaccharides, oxLDL, HMGB1) in sterile inflammation. In pre-clinical models IAXO compounds have been shown to inhibit neuropathic pain; secondary necrosis of acute drug-induced liver failure and vascular inflammation and abdominal aortic aneurysm by blocking non-hematopoietic TLR4 signaling. IAXO compounds hold considerable promise in pharmacological settings, where inhibition of sterile (auto-) inflammation is desired, without compromising TLR4's key role in the defense of pathogens. CD14-dependent and independent TLR4 activation in the central nervous system by endogenous factors has been recently related to a wide array of inflammatory neurological diseases such as amyotrophic lateral sclerosis and Alzheimer's disease.

Product Specific References:

- [1] Glycolipids and benzylammonium lipids as novel antisepsis agents: synthesis and biological characterization. Piazza M, et al. J. Med. Chem. (2009); 52:1209
- [2] Evidence of a specific interaction between new synthetic antisepsis agents and CD14. Piazza M, et al. Biochemistry (2009); 48:12337
- [3] Therapeutic targeting of innate immunity with Toll-like receptor 4 (TLR4) antagonists. Peri F, Piazza M. Biotechnol. Adv. (2012); 30:251 REVIEW
- [4] Exploring the LPS/TLR4 signal pathway with small molecules. Peri F, et al.; Biochem Soc Trans. (2010); 38:1390 REVIEW
- [5] Multivalent glycoconjugates as anti-pathogenic agents. Bernardi A, et al.; Chem Soc Rev. (2013); 42:4709 REVIEW
- [6] Toll-like receptor 4 (TLR4) modulation by synthetic and natural compounds: an update. Peri F, Calabrese V. Med Chem. (2014); 57:3612 REVIEW

DISCLAIMER: THIS PRODUCT IS NOT INTENDED OR APPROVED FOR HUMAN, DIAGNOSTICS OR VETERINARY USE. USE OF THIS PRODUCT FOR HUMAN OR ANIMAL TESTING MAY BE EXTREMELY HAZARDOUS AND MAY RESULT IN DISEASE, SEVERE INJURY, OR DEATH. THIS PRODUCT IS FOR RESEARCH USE ONLY (RUO).

MATERIAL SAFETY DATA: This material should be considered hazardous until information to the contrary becomes available. Do not ingest, swallow, inhale or get into the blood stream. Do not get in eyes, on skin, or clothing. Wash thoroughly after handling. This information contains some, but not all, of the information required for the safe and proper use of this material. Access to this material must be restricted to personnel, who is appropriately experienced, qualified, competent and properly trained to use it. Material Safety Data Sheet is available upon request.