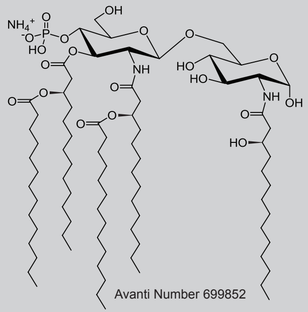
MPLA

3D-PHAD®

Pat No. 9,241,988



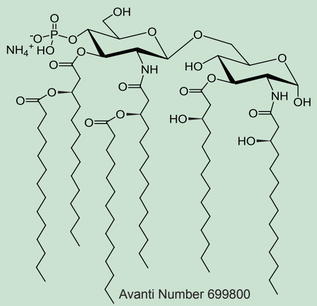
Avanti Number 699852

The highly pure MPLA analog, 3D-PHAD®, provides a homogeneous synthetic equivalent for the 3-deacylated MPLA derived from bacterial LPS. While comparable to bacterial MPLA and other synthetic MPLA analogs at eliciting an immune response in a liposomal adjuvant system (see bar graph), 3D-PHAD® is less pyrogenic than its bacterial-derived mimic. Extensive preclinical testing with 3D-PHAD® demonstrated equivalency to PHAD®, and human trials have been scheduled for launch. 3D-PHAD® is protected under Pat No. 9,241,988. Licensing opportunities are available for vaccine or immunotherapy commercialization.

3D-PHAD®

MPLA

PHAD®



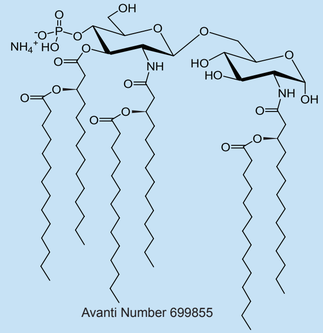
Avanti Number 699800

PHAD® is a synthetic structural analog of monophosphoryl Lipid A (MPLA) that has been shown to boost the immune system through activation of the toll-like receptor 4 (TLR4) resulting in production of proinflammatory cytokines and antigen-specific effector CD4+ and memory CD8+ T cells. Also referred to as GLA, this adjuvant has been administered to well over 1000 human subjects without serious adverse events. PHAD® is available in bulk quantities for vaccine development and commercial manufacturing.

PHAD®

MPLA

3D(6-acyl)-PHAD®



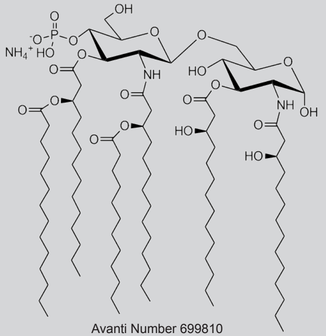
Avanti Number 699855

The MPLA structural analog, 3D(6-acyl)-PHAD®, is the synthetic MPLA most closely related to the reported structure of MPL® Adjuvant used in GSK's Adjuvant Systems AS01, AS02, and AS04. As with other synthetic MPLA analogs manufactured by Avanti, it is structurally homogeneous and highly purified, and mimics the TLR4 agonist activity of bacterial MPLA.

3D (6-acyl)-PHAD®

MPLA

PHAD®-504



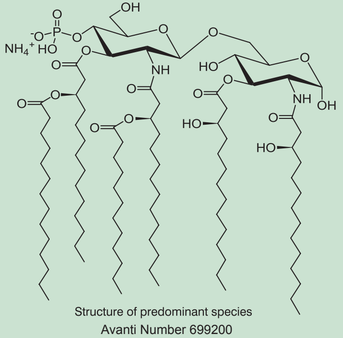
Avanti Number 699810

PHAD®-504 was designed as a synthetic structural analog of detoxified MPLA derived from E. coli lipopolysaccharide (LPS). It is structurally similar to PHAD®, differing only in the length of a single fatty acid chain. As expected, the activity of PHAD®-504 is quite similar to that of PHAD®, making the two products interchangeable as adjuvants in vaccine or immunotherapy formulations.

PHAD®-504

MPLA

Bacterial

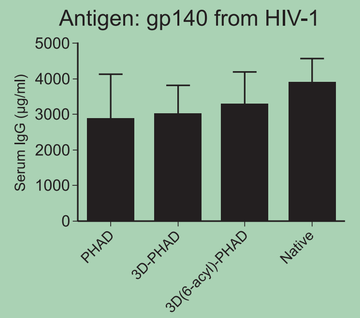


Structure of predominant species
Avanti Number 699200

Avanti manufactures monophosphoryl Lipid A (MPLA) by hydrolysis of endotoxin lipopolysaccharide (LPS) isolated from Salmonella minnesota R595. MPLA is purified from the hydrolysate and contains a mixture of structural analogs containing differing numbers of fatty acids and positional isomers. The detoxified MPLA acts as a toll-like receptor 4 (TLR4) agonist, and hydrolysis of the LPS to yield MPLA retains the activity of stimulating the adaptive immune response while eliminating many of the pro-inflammatory side effects experienced with LPS.

Bacterial

Equivalance of Synthetic MPLA's



Data kindly provided by Dr. Carl R. Alving, Walter Reed Army Institute of Research

PHAD®, 3D-PHAD®, and 3D(6A)-PHAD® have been tested extensively in animals using a variety of antigens. In all cases, these adjuvants exhibit a similar activity and safety profile to bacterially-derived MPL. The data below demonstrate the equivalency of the three synthetic adjuvants to the bacterially-derived MPL when presented in a liposomal carrier system (DMPC/DMPG/Cholesterol).

Equivalance of Synthetic MPLA's

Avanti®
POLAR LIPIDS, INC.

Research Products
Highest Purity Lipid Reagents

cGMP Manufacturing
API & Contract Manufacturing

Adjuvants
Immunotherapy & Vaccine Development

Analytical Services
Lipid Analysis

Lipidomics
Mass Spec Standards, Antibodies & Lipid Toolbox

Formulations
Liposomes & Nanoparticles

Equipment
Liposome Production Tools

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How may we help?

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- Inquiries: adjuvant@avantilipids.com

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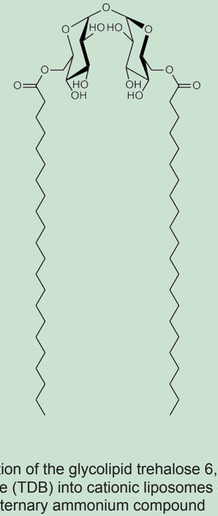
TB Vaccine
Trehalose Dibehenate (TDB)



Incorporation of the glycolipid trehalose 6,6'-dibehenate (TDB) into cationic liposomes composed of the quaternary ammonium compound dimethyldioctadecylammonium (DDA) produce an adjuvant system which induces a powerful cell-mediated immune response and a strong antibody response, desirable for a high number of disease targets.

TB Vaccine TDB

TB Vaccine
DDA

Larrouy-Maumus G, Layre E, Clark S, Prandi J, Rayner E, Lepore M, de Libero G, Williams A, Puzo G, Gilleron M. Protective efficacy of a lipid antigen vaccine in a guinea pig model of tuberculosis. Vaccine. 2017 Feb 9. pii: S0264-410X(17)30159-7.

Derrick SC, Yabe I, Morris S, Cowley S. Induction of Unconventional T Cells by a Mutant Mycobacterium bovis BCG Strain Formulated in Cationic Liposomes Correlates with Protection against Mycobacterium tuberculosis Infections of Immunocompromised Mice. Clin Vaccine Immunol. 2016 Jul 5;23(7):638-47.

Rose F, Wern JE, Ingvarsson PT, van de Weert M, Andersen P, Follmann F, Foged C. Engineering of a novel adjuvant based on lipid-polymer hybrid nanoparticles: A quality-by-design approach. J Control Release. 2015 Jul 28;210:48-57.

Teng X, Tian M, Li J, Tan S, Yuan X, Yu Q, Jing Y, Zhang Z, Yue T, Zhou L, Fan X. Immunogenicity and protective efficacy of DMT liposome-adjuvanted tuberculosis subunit CTT3H vaccine. Hum Vaccin Immunother. 2015;11(6):1456-64.

TB Vaccine DDA

Adjuvant Formulations

Is your immunotherapy or vaccine program spending valuable time and resources on adjuvant formulation development? With nearly 100 years of combined experience formulating lipids, Avanti can support your adjuvant formulation development activities. We offer formulation services for both pre-clinical and clinical development using our own cGMP manufactured lipids. Batches can be scaled from a few milliliters to >100 liters to accommodate your stage of clinical development. We work closely with your packaging group throughout the process to ensure we provide material suitable for aseptic fill/finish in your final dosage form for clinical trial. When you are ready for commercialization, Avanti can work in partnership with your CMO to provide a seamless transfer of the formulation for scale-up and manufacturing.

Discover the Difference

Adjuvant Formulations

Licensing Opportunities

Vaccine adjuvants using heterogeneous monophosphoryl Lipid A (MPL) derived from Salmonella minnesota R595 have proven to be safe and effective at inducing Th-1 type immune responses to heterologous proteins in animal and human vaccines. Avanti revolutionized immunotherapy and vaccine development with the introduction of Synthetic MPL derivatives and adjuvant systems. Avanti now manufactures multiple synthetic analogs of MPL containing a single molecular species that are as effective and safe at inducing an immune response as their natural product predecessor. PHAD®, 3D-PHAD®, and 3D(6A)-PHAD® are manufactured according to cGMP guidelines and are available in bulk quantities for your clinical trials. Licensing opportunities are available for your field of use. Contact adjuvant@avantilipids.com for more information.

3D-PHAD®, Pat No. 9,241,988

People do
amazing
things with our lipids.
What will **you** do?

Licensing Opportunities

Avanti®
POLAR LIPIDS, INC.

Lipid Based
Adjuvant System

Immunotherapy & Vaccine Development

More than Lipids

Solutions for the entire product cycle: research to commercialization.

photo provided by: Kyriakos Kazmas