Polyethylene Glycol (PEG) Micelles with Cholesterol Provide an Improved Delivery System for AmB

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THE WARF ADVANTAGE

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OVERVIEW

Systemic fungal infections are a significant and often life-threatening clinical problem, particularly in patients with a suppressed immune system. The drug of choice for treating these infections is Amphotericin B (AmB), a broad spectrum antifungal agent that acts by disrupting fungal cell walls. But AmB is extremely toxic, poorly soluble in water and difficult to formulate and administer. UW-Madison researchers previously demonstrated that AmB could be made soluble and deaggregated by PEG-DSPE micelles, resulting in substantial reduction in toxicity in vitro; however, only modest reduction in toxicity occurred in vivo.

THE INVENTION

UW-Madison researchers have now developed an improved micellar delivery system for AmB. The system uses PEG-DSPE micelles in which cholesterol has been incorporated to structure the micelles. When AmB is encapsulated within PEG-DSPE micelles, the hydrophilic exterior interacts with the aqueous environment while AmB, a hydrophobic molecule, resides within the core. This increases the solubility of AmB, leading to lowered toxicity and increased efficacy. When cholesterol is added to the micelles, AmB is released slowly in the presence of bovine serum albumin, suggesting that it would be less toxic in vivo. In addition, this formulation is stable in the presence of NaCl, which is given to patients to protect against the dose-limiting kidney toxicity caused by AmB.

APPLICATIONS

• Controlled delivery of AmB
• Controlled delivery of other pharmaceutical compounds, including rapamycin
• Treatment of fungal infections, including candidiasis, cryptococcoses, aspergillosis, histoplasmosis, blastomycosis and coccidiomycosis
KEY BENEFITS

- Formulation reduces host toxicity while retaining AmB’s potent antifungal activity.
- AmB is readily incorporated into these micelles.
- Because this formulation is compatible with aqueous salt solutions, it allows for concurrent sodium supplementation and/or co-administration of other pharmaceutical agents.
- In addition to cholesterol, other sterols, such as ergosterol, lanosterol, beta-sitosterol or stigmasterol, could be used.
- Micelles are unique among drug carrier systems due to their nanoscopic dimensions, hydrophilic shell and hydrophobic core.
- Micelle compositions are easy to store and deliver, circulate in the blood for a long time, are excreted by the kidneys and can be targeted to specific locations within the body.

ADDITIONAL INFORMATION

Publications


Tech Fields

Drug Discovery - Drug delivery
Pharmaceuticals & Vitamin D - Antibacterials

CONTACT INFORMATION

For current licensing status, please contact Mark Stoveken at licensing@warf.org or (608) 263-2500.