**Abstract**

One of the most common serious diseases of the developing world is almost unknown in this country. It is *Leishmaniasis*, also known as *kala-azar*. After malaria, this is the most common fatal parasitic infection in the world. It is difficult to treat and has demonstrated increasing rates of resistance toward many main-line drugs. Fortunately, there is a drug which is very effective, almost never generates resistance and is very inexpensive—Amphotericin B (AmB).

The problem is that this drug is not available in a stable oral form which would be advantageous in tropical climates. The most common preparation of AmB is administered intravenously as a micellar dispersion. This dispersion shows poor selectivity between mammalian and parasite cells and hence increased human toxicity. However, by employing lipid carrier complexes, a formulation can be implemented to control the toxicity, specificity, solubility, and stability of this drug and improve digestive tract absorption. Our objective was to develop and establish procedures for testing and characterization of novel orally-available lipid drug delivery formulas for AmB. We have evaluated these and other lipid mixtures by stopped-flow spectroscopy to clarify the relationship between composition and drug activity in in vitro model systems.

**Amphotericin B**

A polyene antifungal drug commonly used to treat systemic fungal and parasitic infections

**Anti-fungal Properties:**
- Preference for ergosterol in cell membrane
- Transmembrane channel formation leads to ion leakage

**Problems:**
- Poor sterol selectivity
- High toxicity
- IV infusion required
- Degradation with exposure to light
- Associated with high fever, chills, nausea, etc.

**Lipid & SEDDS Formulations**

Self-Emulsifying Drug Delivery Systems (SEDDS):
- Mono- and Di- glycerides and PEG esters that form emulsions spontaneously in stomach and gastrointestinal fluid

**SEDDS Characteristics:**
- Can emulsify hydrophobic drugs
- Can carry hydrophobic drugs into the lymph or blood circulatory system
- Allows oral absorption of Amphotericin
- Reduces toxicity of some drugs

**Benefits of orally available systems:**
- Reduced toxicity
- Cost effective
- Stable at room temperature
- No hospitalization or IV infusion

**Current Formulations of Amphotericin:**
- Exist as lipid-complex mixtures
- Ambisome and Amphotec exhibit reduced toxicity compared to Fungizone
- Still must be delivered intravenously
- Stability in serum is correlated with lower toxicity

**Measuring Drug Stability with Stopped-Flow Spectroscopy:**

Dissociation of Amphotericin is measured by a shift in wavelengths from short wavelength aggregated from to long wavelength monomer form

**Conclusions**

- Reduced stability of Amphotericin in serum can be shown by Stopped-Flow Spectroscopy
- Future studies on SEDDS will determine whether stability correlates with toxicity reduction and oral delivery

**References**


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