P0013
Poster Session I
News from the fungal frontier

COMPARATIVE STABILITY ANALYSIS OF TWO COMMERCIAL AMPHOTERICIN B FORMULATIONS: LIPOSOMAL (AMBISOME) AND LIPID COMPLEX (ABELCET)

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OBJECTIVE:

Liposomes formulated to act as drug carriers should be prepared from phospholipids with Tcs above 37ºC in order to be stable with minimal toxicity, as it is the case of liposomal amphotericin (Adler Moore J 2002). To perform a comparative study of amphotericin B (AmB) stability in two commercial lipid formulations (Ambisome and Abelcet) during the process of preparing the drug for administration and subsequent storage, and to evaluate the stability during a process of IV administration simulation.

METHODS

We studied the stability of lipid-bound AmB and presence of free AmB in 5% glucose solutions (concentration: 1 mg/ml) when exposed to the following conditions:

- Gentle or vigorous agitation of drug vial

- Use or nonuse of filter in the syringes used for solution preparation

- Storage temperature: 4 and 25ºC

- Storage time: short term: 0, 1, 2, 4 hours; long term: 8, 24 and 48 hours

- Effect of sample warming to 37ºC over the following times: 0, 1, 2, 6 hours and long term: 24 hours, 3, 6 and 10 days.

The levels of lipid-bound AmB and free AmB were quantified by previously validated HPLC-UV methods. Free AmB is listed as a percentage of the initial concentration.

RESULTS

Various conditions to which the samples were exposed led to small free fractions in both cases; 8% in Ambisome and 1% in Abelcet. No significant differences in the percentage rate of free fractions were observed for each antifungal between the various types of agitation, filter use in the syringes, solution storage temperature (4 or 25ºC) and short term storage time.

However, the long-term stability of each formulation was different as of the first 8 hours. Whereas the liposomal AmB concentration remains constant, AmB in lipid complex was significantly reduced ($p<0.001$) as of the first 8 hours: 3.3% reduction in Ambisome and 30.0% in Abelcet. In addition, some tendency toward a decrease over time in free AmB concentration in the two formulations was observed, but the impact on both cases was minimal and consistent with a spontaneous drug degradation process.

Warming the solution from the storage temperature (4ºC or 25ºC) to 37ºC led to very different behaviors in both formulations and free Abelcet fraction highly increased compared to AmBisome as of the first hour (231% at 24 hours compared to initial free AmB (0 h)). (Table 1)

CONCLUSIONS:

At 37ºC regardless of the conditions used to prepare the AmB solutions using the two formulations tested, Ambisome solutions are highly stable compared to Abelcet solutions, which are poorly stable. The lipid fraction of Abelcet decreases as of 8 hours, and the formation of free AmB of Abelcet highly increases compared to AmBisome when the solutions are exposed to body temperature.

Table 1. Percentage of free AmB in samples after warming at 37ºC

Vial	Gentle agitation		Vigorous agitation		Gentle agitation		Vigorous agitation	
Transfer	Filter	No filter	Filter	No filter	Filter	No filter	Filter	No filter
	4ºC				25ºC			
	Ambisome							
1 h	6.84%	-21.6%	-29.6%	-31.7%	-13.9%	-2.05%	-13.1%	-3.34%
2 h	8.91%	-3.74%	-28.6%	-15.9%	-19.6%	-2.3%	-7.43%	-12.9%
6 h	12.43%	-9.93%	-37.8%	-29.6%	-17.6%	-4.23%	-5.67%	-20.9%
24 h	-1.37%	-6.66%	-9.02%	-22.3%	5.06%	20.79%	3.06%	-7.69%
3 d					-37.1%	-28.9%	-43.4%	-35.8%
6 d					-31.7%	-11.0%	-36.6%	-38.8%
10 d					-36.4%	-32.3%	-57.8%	-35.8%
	Abelcet							
1 h	41%	45%	84%	25%	68%	49%	77%	52%
2 h	242%	67%	106%	36%	94%	80%	91%	73%
6 h	267%	109%	152%	78%	184%	128%	160%	117%
24 h	362%	168%	237%	130%	223%	231%	237%	258%
3 d					222%	188%	211%	242%
6 d					264%	245%	260%	261%
10 d					363%	259%	359%	278%