Homogenizer, Model 15M was used. The modification consists of two heat exchange reservoirs that maintain the lipid solution at a selected temperature. In the operation, the solution is subjected to very high shearing forces in the homogenizing valve area while maintaining the solution at a selected temperature. A certain period of time is selected to allow multiple circulations of the entire lipid solution through the homogenizer. The final product can be readily sterilized by aseptic filtration. The microemulsification procedure produced small liposomes with less toxicity and a more consistently homogeneous size distribution than sonicated liposomes (Adler-Moore and Proffitt, 1993). Electron microscopic examination of the AmBisome by negative staining and freeze fracture confirmed the small, unilamellar, and spherical morphology of the liposomes (Adler-Moore and Proffitt, 1993).

AmBisome is a sterile, lyophilized powder with a shelf life of up to 4 years when stored at or below 25°C. This form can be easily reconstituted by adding sterile water and shaking by hand. The physicochemical and biological properties of the rehydrated products do not change during this time. The amount of drug association with the liposomes was confirmed by applying AmBisome to a Sephadex G25M chromatographic column. All the amphotericin B was recovered from the liposomal fraction of the column (Adler-Moore and Proffitt, 1993).

AmBisome has proven its efficacy in both controlled and randomized clinical trials. There are more than 150 publications on the safety and efficacy of AmBisome in the treatment of life-threatening fungal infections. The incidence of adverse effects for AmBisome is low, namely, 5%–10%, compared with 80% of the conventional amphotericin B formulation. The effective dose for AmBisome ranges from 1 to 3 mg/kg and achieves peak liposomal amphotericin B level of 29 μg/mL at 1 mg/kg dose, compared to 3.6 μg/mL for the conventional amphotericin B at the same dose. AmBisome is well tolerated when used with Cyclosporin A, an important consideration when treating organ transplant patients. AmBisome can be administrated rapidly, usually within 30–60 min, and without need for administering a test dose or pretreating patient with antihistamines or fever-reducing agents. To date, AmBisome has been used to treat more than 100,000 patients worldwide.

Doxorubicin

Doxorubicin is a cytotoxic anthracylcine chemotherapeutic agent isolated from cultures of *Streptomyces peucetius*. The cytotoxic effect is thought to be related to its ability to intercalate between nucleotide bases of DNA and RNA of target cells, thereby inhibiting nucleotide replication and action of DNA and RNA polymerases. It has been used for a variety of malignancies and cancers such as disseminated neoplastic conditions such as acute lymphoblastic leukemia, acute myeloblastic leukemia, neuroblastoma, soft tissue and bone sarcomas, breast cancer, ovarian cancer, Hodgkin's disease, malignant lymphoma, AIDS-related Kaposi's sarcoma, and multiple myeloma. However, it has several adverse side effects, most notably cardiotoxicity, that significantly limit its dosage. The cardiotoxic effects include cumulative dose-related congestive heart failure, left ventricular ejection fraction, and histological changes (Rahman et al., 2007). Hence, liposomes have been successfully investigated to ameliorate the cardiotoxic effects of doxorubicin, to enhance preferential uptake by tumor cells rather than cardiac tissue. Whereas blood vessels in cardiac tissues have tight capillary junctions, those in tumors allow more extravasation of species such as liposomes into the tumor, which enhances uptake of a liposome-encapsulated chemotherapeutic agent into the tumor (Green and Rose, 2006). Doxorubicin liposomes were first examined clinically as early as the 1980s (Rahman et al., 1990). Doxil (US; Caelyx® in the EU) a long-circulating (pegylated) doxorubicin liposomal formulation, was approved in 1995 for Karposi's sarcoma, and in 1999 for ovarian cancer. A non-pegylated lipsomal formulation, Myocet, was approved in Europe in 2000 (Barenholz, 2012; Allen and Cullis, 2013). For Doxil, Phase III trials showed similar efficacy compared to conventional doxorubicin, but had a superior safety profile, with lower incidence of alopecia, myelosuppression, nausea and vomiting, and a significantly lower incidence ($p < 0.001$) of cardiotoxicity even at higher cumulative doses (Rivera, 2003). Liposomal encapsulation has a large