GMP/LARGE SCALE PRODUCTION OF LIPOSOMAL THERAPEUTICS AND VACCINES

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Over the past few years liposomal drug preparations have been increasingly used in clinical trials. These clinical trials have guided liposomes from laboratory research to clinical reality with very encouraging results. For all these products, a simple, economic and GMP-conform production technique and facility is necessary. Based on the ethanol injection technique, we have realised a scalable and sterile production technique. Continuous aseptic one-step operation permits the production of stable and sterile liposomes with a defined size distribution. By using this technique, several products are now in preclinical or clinical stage. One of these is a liposomal/virosomal vaccine against HIV. Encapsulation rates of membrane proteins up to 95% could be observed and ongoing preclinical in vivo studies show promising results. In the vaccine section we also worked on the efficient passive entrapment of peptides for a partner company where we nearly doubled their previous encapsulation rates. In the liposomal therapeutics field, we realised a one step remote loading technique. With this method galanthamine hydrobromide, currently used for the treatment of mild Alzheimer disease, was loaded into liposomes for the treatment of peripheral neuropathies. A double blind randomised phase 2 trial is currently being performed. Last but not least, the liposomal rh-Cu/Zn-SOD (Lipoxysan) has finished phase 3 trials for the topical treatment of induratio penis plastica (IPP) with very encouraging results. In addition, case studies for the treatment of chronic ulcers are currently going on and nebulised, pulmonary applied liposomal SOD is currently investigated in a pig model for the treatment of acute respiratory distress syndrome (ARDS). In conclusion, liposome manufacture with the crossflow technique is suitable for the production of liposomal vaccines and therapeutics. The main advantage of this technique is the feasibility of manufacturing batches of 5-10 ml, which is directly scalable to several litres. This variant avoids cost-intensive scale-up and permits early prognosis about product quality, thus liposomes can be screened more quickly and more efficiently. This is of particular importance when it comes to cost-intensive drugs that are to be manufactured by novel biotechnological procedures.
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