1 Relevance of Liver Support

Each year in the U.S., approximately 150,000 people are hospitalised with liver disease and over 43,000 people die from it (Langer and Vacanti 1993). These numbers are expected to increase as the 4 million people currently infected with Hepatitis C advance to liver failure. Transplantation, the only effective means of treating liver failure, is not an option for many patients. Some are simply not sick enough to justify the massive cost, invasiveness and risk of a transplant, leaving them unaided today. Other patients are too sick to qualify, while others die awaiting a transplant.

Ironically, the liver is a highly regenerative organ (Michapoulos 1990). Some patients currently undergoing liver transplantation would not need this major surgery if there were a simpler means of obtaining
liver function until their own organ had recovered. Over the past 30 years, various supportive therapies for patients with acute liver failure have been proposed. Detoxification-based methodologies for liver support such as dialysis, haemofiltration and haemoperfusion have proven ineffective because physical methods are not sufficient for the management of severe biochemical disorders.

Unlike other organs (lung, kidney, heart) which have one primary function, the liver has multiple functions essential to maintain life, including carbohydrate metabolism, synthesis of proteins amino acid metabolism, urea synthesis, lipid metabolism, drug biotransformation and waste removal.

To address the critical medical needs of liver-compromised patients, the development of an extracorporeal liver-assist device, using isolated liver cells, to which patients would be temporarily connected until they recovered or received a liver transplant, could be a promising approach. Components of the patient’s blood are to be passed through the device, processed by living liver cells within the device and then returned to the patient using a dialysis-type procedure.

Since fulminant liver failure is potentially reversible, the extracorporeal bridging of liver function would also be beneficial until the patient’s own liver resumed functional activity.

2 Development of Bioartificial Liver

Recent developments in tissue engineering have made it possible for us to use isolated hepatocytes in a bioreactor for the creation of a bioartificial liver, which supports patients with acute liver failure. Isolated hepatocytes retain tissue-specific functions and may able to correct metabolic imbalances while providing specific factors for liver regeneration. Since fulminant liver failure is potentially reversible, extracorporeal bridging of liver function would also be beneficial until the patient’s own liver resumed functional activity. In recent years, different bioreactor systems have been developed. They can be classified according to the immobilisation technique used: microcarriers (Demetriou et al. 1986), hollow-fibre membranes (Gerlach et al. 1994), flat-sheet membranes (Bader et al. 1998), biological matrices (Bucher et al. 1990), non-woven polyester matrix (Flendrig et al. 1997) and encapsulation