A Hepatocyte Bioreactor Using In Situ Immobilization Method

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Despite recent advances in medical supportive therapy, patients with severe fulminant hepatic failure (FHF) have mortality rate approaching 90%. To treat such patients, investigators have attempted to improve neurological status and survival rate by using various extracorporeal bioartificial liver (BAL) systems. The BAL will act as a bridge to provide patients with more time until a donor organ became available for transplantation or until their own liver can be regenerated.[(1)] Several requirements should be met for the BAL systems: (1) hepatocytes should be cultured in sufficiently high cell density; (2) their metabolic functions should be of sufficiently high level and duration; and (3) the BAL system module should permit scaling-up and aseptic handling.To satisfy a BAL system for clinical use, more than 10% of total human liver cells (about 2×10^{10} cells) are required

In the conventional immobilization process utilizing sodium alginate, cells are entrapped as bead type by dropping alginate cell solution into Ca ion solution. If the cells were immobilized with extremely high density, size of the Ca-alginate bead was minimized to prevent central necrosis due to hypoxia.[(2)]

In this study, we developed novel in situ immobilization method using wettable surface and alginate. As a Ca-donating wettable substrate we chosen the gauze and that were arranged with 1 mm interval in the perfusion bioreactor. Ca-Alginate gel layer was

simply formed on the surface of gauze by injecting the alginate-hepatocyte solutions into the bioreactor. In this configuration fabricated by the in situ immobilization, central hypoxic region was occupied by gauze fibers. Therefore, hepatocytes could be immobilized with higher cell density. In conclusion, this simple immobilization method can offer useful alternatives for the development of hepatocyte bioreactor for BAL system application.

References

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