

6. Summary

Effects of matrix- and capsule modification on the functional survival of microencapsulated islets of Langerhans in vitro

Despite insulin therapy transplantation of immunoisolated islets of Langerhans is investigated as treatment for type 1 diabetes. However oxygen supply plays a crucial role for graft survival and function. In previous studies we could demonstrate, that immobilized hemoglobin inside the capsule matrix leads to a significantly increased function and viability of microencapsulated islets. Because a more efficient oxygen supply caused by hemoglobin could be excluded, the present study investigated, whether the iron contained in the Hb molecule is responsible for the positive effect of Hb. This was realized by substitution of Fe^{2+} and Fe^{3+} cations in the precipitant for alginate ($BaCl_2$) on the one hand and by immobilization of iron-containing factors inside the capsule matrix Transferrin (Tf), erythrocytes (Ery), hemolysated erythrocytes (hEry), Hemoglobin (Hb), and Albumin (Alb) on the other hand.

Ba-alginate microencapsulated neonatal rat islets were used as control group.

The absolute insulin secretion, the relative stimulatory response to glucose and the viability before and after 4 weeks of culture was determined.

During the culture period insulin secretion declined in all groups investigated.

The absolute insulin secretion of the Hb-containing group and of the Alb-containing group, however, was significantly increased ($p < 0.05$) compared to the control group. Furthermore the Albumin modification resulted in a significantly higher stimulatory responsiveness to glucose and in the best viability compared to all other groups. Because albumine doesn't contain any iron, an iron-mediated improvement of oxygen supply may be excluded. Other factors like an unspecific protein action may have taken effect.

Ery-, hEry-, Fe^{2+} -, Fe^{3+} -, Tf-containing microcapsules have shown no beneficial effect on function and survival of microencapsulated neonatal rat islets.

This may be due to technical problems during the microencapsulation process of the Tf- and Ery- containing capsules (solubility of Tf in alginate, conglomeration of erythrocytes, increased viscosity of the alginate matrix etc.).

The beneficial effect of immobilized Hb inside the alginate matrix of micro-encapsulated islets as be shown in former investigations could be reproduced by the present data. This effect, however, may be caused by other factors than by iron.