IN VITRO EFFECTS OF ANTI-INFLAMMATORY DRUGS INCORPORATED IN SOLID LIPID NANOPARTICLES ON HUMAN PERIPHERAL MONONUCLEAR BLOOD CELLS FROM IBD PATIENTS

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The ordinary treatment of inflammatory bowel disease (IBD) require the frequent intake of anti-inflammatory or immunosuppressive drugs at high doses, which causes significant adverse events. Therefore, a carrier system that delivers the drug specifically and exclusively to the inflamed regions for a prolonged period would be desirable.
Solid lipid nanoparticles (SLN) are being extensively studied as promising alternative carriers for drugs. SLN, prepared from a warm microemulsion, can increase bio-availability and modify pharmacokinetic parameters and tissue distribution of the incorporated drug.
Dexamethasone is a glucocorticoid that is used clinically as an anti-inflammatory and immunosuppressive agent and its controlled delivery is highly desired to avoid the side effect of chronic use.
Butyrate, a short chain fatty acid normally present in the body, has been used for the treatment of various inflammatory diseases. However the infrequent application is not due to side-effects or general toxicity, but to the extremely short half life of butyric salts derivatives, which impairs any long-lasting effect *in vivo.* For this reason, a particular SLN formulation, cholesteryl butyrate (chol-but) SLN, have been developed.
In this work, we evaluated the capacity of SLN to improve activity of anti-inflammatory drugs, such as dexamethasone and butyrate, *vs* commercial formulations, by studying the effects on proliferation, mRNA expression and cytokine secretion of human peripheral mononuclear blood cells (PMBC) from blood samples of IBD patients.
The concentrations of IL-1beta, TNF-alfa, IFN-gamma and IL-10 in culture supernatants of PMBC were measured using ELISA assay and the expression levels of cytokines mRNA were measured using quantitative SYBR Green real-time RT-PCR.
The secretion and mRNA expression of IL-1beta ($p<0.01$), TNF-alfa ($p<0.05$) and IFN-gamma ($p<0.01$) was significantly decreased while IL-10 ($p<0.05$) secretion and mRNA expression was significantly increased by chol-but SLN at the highest concentration tested (40 microM).
The secretion and mRNA expression of IL-1beta ($p<0.001$), TNF-alfa ($p<0.001$) and IFN-gamma ($p<0.05$) was significantly decreased while IL-10 ($p<0.05$) secretion and mRNA expression was significantly increased by dexamethasone SLN at the highest concentration tested (100 ng/ml).
Moreover, no cytotoxic effects have been reported at the highest concentration tested able to inhibit cytokines production.
In conclusion, these data suggest that incorporation in SLN of dexamethasone and butyrate significantly improve *in vitro* drug anti-inflammatory effects.