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

Serpe Loredana¹, Canaparo Roberto², Daperno Marco³, Eandi Mario¹, Gasco Maria Rosa⁴ and Zara Gian Paolo¹

¹Department of Anatomy, Pharmacology and Forensic Medicine, University of Torino, Torino,
²Department of Clinical Pathophysiology, University of Torino, Torino,
³Department of Gastroenterology, Mauriziano Hospital, Torino,
⁴Nanovector s.r.l, Torino

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.