SILICA MICROPARTICLES FOR THE CONTROLLED RELEASE OF HUMAN GROWTH HORMONE

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The increasing interest in sustained-release formulations of therapeutic proteins is well justified. Such systems can provide greater safety and efficacy and improve patient compliance because of less frequent administration.
In this work, we propose a novel slow-release formulation of h-GH based on silica microspheres composed of wet sol-gel derived silica gels.
Human Growth Hormone (h-GH) was entrapped in various formulations having different silica contents (12%, 14%, 15%, 16% wt/v) and protein loading (0,6 to 1,2 %). Silica microparticles were characterized by optical microscopy, while conformational stability of h-GH entrapped and released was analyzed by circular dichroism.
To assess if microparticles manufacturing conditions affect protein bioactivity, a cell proliferation assay was conducted incubating Nb211 cells with h-GH solutions, released by silica microparticles in physiological conditions.
Since *in vitro* release tests demonstrated a slow and gradual release of h-GH, microparticle suspensions were then administered to Sprague-Dawley male rats to evaluate pharmacokinetic profiles. These were assessed by determining h-GH levels in plasma at different times and by ELISA assay. These *in vivo* experiments show how optimized formulations of silica microparticles provide consistent levels of h-GH for a period of 72h after a single sc administration, with a 10 fold increase in protein half-life compared to single sc injection of unmodified h-GH.
In vitro and *in vivo* data obtained so far look very promising for the development of a sustained-release formulation for parenteral administration of h-GH or other therapeutic proteins, since the maintained bioactivity of the entrapped protein has been demonstrated together with prolonged-release in male rats as animal model.