SLOW RELEASE OF WATER-SOLUBLE DRUG FROM A BIODEGRADABLE AND BIOCOMPATIBLE POLYMER MATRIX. APPLICATION TO THE SUPEROVULATION IN COWS.

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The classical treatment to induce superovulation in cows consists in intramuscular injections of porcine Follicle Stimulating Hormone (pFSH) and porcine Luteinizing Hormone (pLH) every 12 hours for 4 days. However, this type of treatment has many disadvantages as the number of injections, loss of time, and a repeated stress for the cow , which can be prejudicial to good superovulatory responses. By using a specific and sensitive radioimmunoassay, the pulsatif pFSH profile induced by the classical superovulatory treatment was determined. From this profile, the half-life (t1/2) of pFSH and the mean pFSH plasmatic concentration were estimated to be respectively 5 hours and 0,3 ng/ml.
To avoid the disadvantages of the classical treatment, we developed a sustained release system for these water-soluble glycoproteins (pFSH; pLH). This system had to release all the drug on 4 days and induce a mean pFSH plasmatic concentration near to 0,3 ng/ml. Moreover, it had to be biodegradable.
Therefore a physical mixing in well determined proportions of glycoproteins and polylactide 50 (PLA50), was extruded under the form of a rod. It was injected with a trocar in the ear of the cow.
The system released all the drug on approximately 100 hours and induced a maximum pFSH plasmatic concentration near to 0,3 ng/ml.
The test of Steelman and Pohley prooved that the biological activity of glycoproteins introduced in the matricial system was preserved and that the biological response was more reproducible for the matricial system than for the repeated injections
The biocompatibility of the system was tested on rats and only a slight inflammatory reaction was observed.
The matricial system was porous and released the drug by diffusion through the gaps.
It was in vivo slightly slower degraded than the PLA50 alone: on 21 days, the system lost 17% of its molecular weight against 27% for the PLA50.
In summary, as the elaborated system meet all the imposed conditions, it could be suitable to induce superovulation in cows.