ImmunoTools *special* Award 2014

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Biocompatibility Evaluation of an Innovative Thermo-sensible Carbomer-based Hydrogel for Drug Delivery

Regenerative medicine seeks to devise new therapies for patients with severe injuries or chronic diseases in which the body's own responses do not provide recovery of complete functions. In order to address this task, one of the most widely applied strategies is the development of smart materials, which are able to release drugs *in situ*. Therefore there has been considerable interest in formulations which exhibit the properties of polymer solutions outside of the body (allowing easy injection), but gel *in situ* within the body.

During the last year I've been working on the modification of the formulation of a semisynthetic hydrogel, synthetized by the copolymerization of two polymers: agarose and carbomer. The purpose was to improve the characteristics of the hydrogel in order to release a particular molecule, resveratrol. This molecule has demonstrated numerous therapeutic effects *in vitro*, such as anti-oxidant, anti-inflammatory, cardioprotective and neuroprotective activity. Although *in vitro* studies have pointed to its large therapeutic properties, this molecule is characterized by some disadvantages that limit its bioavailability *in vivo*, such as low stability, low solubility in water, and consequently in biological fluids, and rapid metabolization, which determines a low concentration in the systemic circulation. The therapeutic potential of resveratrol *in vivo* can therefore be appreciated only if such limitations are exceeded. The solution that I adopted in my study to increase the bioavailability of this molecule is the use of hydrogels as controlled release systems. The advantage given by the selected hydrogel is that it is easily injectable, since it exhibits the properties of a polymer solution over 40°C and it gels in correspondence of the body temperature.

Therefore I studied the characteristics of the agar-carbomer hydrogel and I modified its formulation in order to improve the *in vitro* cytocompatibility of the material. On the other hand, I also evaluated the rheological behaviour and the hydrogel stability. The goal of my study was to obtain a formulation which combined a good *in vitro* cytocompatibility and the most suitable rheological characteristics for the cited application.

After finding the formulation that meets all the requirements, preliminary release tests of resveratrol were made. The results show that the hydrogel is able to release the half of the resveratrol loaded within the first 24 hours and at the end of the tests (7 days) the hydrogel releases the 80% of the drug.

The results obtained *in vitro* suggest the possibility to investigate the effect of the material *in vivo*. Therefore, the use of specific antibodies from ImmunoTools related to murine immune reaction could be useful to evaluate if the material subcutaneously injected in recipient mouse determines or not an inflammatory reaction and if it influences the biochemical signalling of the adjacent tissues and cell-to-cell cross talking. This could be a great opportunity to extend the research.