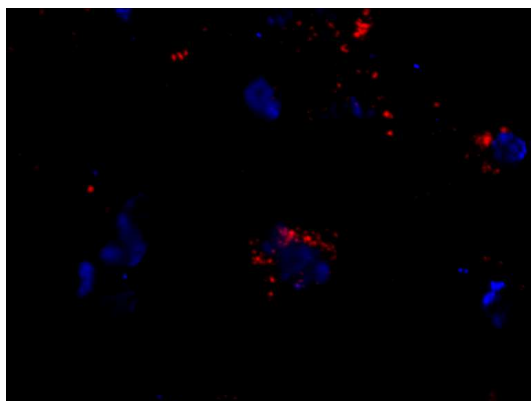


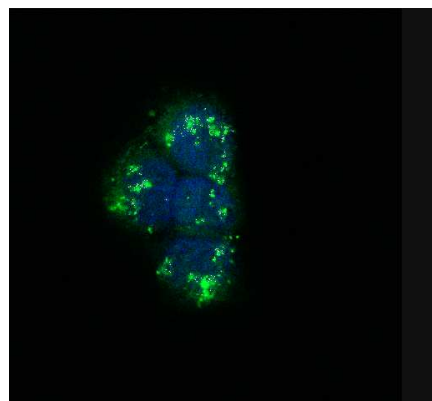
Smart nanocarriers for the drug delivery

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One of the most stimulating challenge in the pharmaceutical sciences is represented by the delivery of drugs in the correct site, in a suitable dose and for a defined time. This challenge has been investigated by using both lipid and solid nanocarriers, such as nanoparticles (Np) and liposomes (L), with the aim of obtaining vectors able to improve the pharmacological activity of drugs against cerebral disease and for the delivery of genetic material. As an example, specific drugs used in the therapy of cerebral diseases find a great difficulty in developing their activities and a field of research is directed to the use of Np as drug carriers for the CNS drug delivery with *in vivo* proofs of their efficacy. An application of the use of lipid nanocarriers consists in offering drug protection and facilitating internalization of genetic materials; new lipid systems were demonstrated to be able to transfect efficaciously different cells lines. Particularly, novel L formulations have demonstrated a good *in vitro/in vivo* stability and improved efficacy and safety of the therapeutic systems.



Confocal microscopy: Modified fluorescent Np in brain parenchyma after a systemic administration



Confocal microscopy: HaCaT cells after new L/ODN complex transfection. Co-localization studies.

1. Description of the product

As an example of nanotechnology applied to the drug delivery to the CNS it is important to know that at present, only invasive methods such as intracranial injections, or the use of prodrugs are available for drugs unable to cross the BBB. This research has developed Np obtained starting from a polymer, poly(D,L-lactide-co-glycolide), approved by FDA. This polymer has been modified with short peptidic sequences and the new polymeric materials obtained are able to form Np that cross the BBB, to disguise the membrane limiting characteristics of the drug molecules and to be used in different pathologies of the CNS. Considering the “gene trouble”; the most important problem is the realization of efficient carrier systems able to protect gene material and to ensure cell internalisation.

2. Innovative aspect of the product

For the preparation of polymeric Np, a new aspect of the product is the punctual chemical modification of the polymer with specific molecules, chosen with the aim of the obtainment of a carrier for CNS. PLGA conjugation with BBB specific ligands were obtained in a simple synthetic method, allowing a possibility for industrial scale up, obtaining Np with modified surface characteristics, able also to bypass hepatic uptake and target CNS district crossing BBB. For the preparation of L, neutral and cationic lipids, and some derivatives from bile acids with stabilizer and cytoprotective characteristics, were used. In particular, cationic Ls, created by the addition of UDCA (with a decreased associated toxicity) have demonstrated to be

good carriers for oligonucleotide in HaCaT (keratinocytes cell line) cells. Recently, we obtained a new stable cationic pegylated anti-CD138 liposomes (ILp) with good physicochemical properties potentially able to efficiently encapsulate and deliver a model oligo against an aggressive B-cell non Hodgkin lymphoma, a Primary Effusion Lymphoma (PEL). In this case, the innovative aspects in the development of ILp are the optimization of both the encapsulation and the surface modification, to improve the efficacy on drug targeting.

3. Main advantages of the offer

If considering the Np, modified PLGA can be considered as a starting material, biodegradable, biocompatible, a-toxic and a-carcinogenic polymer, approved from FDA; the material allow a large scale production. The industrial and clinical applications of these new materials will improve the existing therapies, so the industrial interest of this product is destined to sanitary industries, above all in pharmaceutical research areas and it should be sustained by the necessity to improve and increase the existent therapies. Taking into consideration the L, the industrial sphere is the bio technologic-sanitary one which would like to develop innovative pharmaceutical formulations for gene therapy.

4. Technology key words

Nanoparticles, Liposome, Monoclonal Antibody, Brain Targeting, Gene Therapy.

5. Current Stage of Development

Work in progress – Laboratory tested (in vivo (rat) and in vitro assays): fluorescent assays; pharmacological assays.

6. Intellectual Property Rights

The product of the research is covered by patent.

Technical and scientific publications

G. Tosi, et al. In vivo experiments with peptide derivatized nanoparticles loaded with Loperamide and Rhodamine 123, J. Control. Rel., 122, 1-9, 2007.

G. Tosi, et al, Polymeric nanoparticles for the drug delivery to the central nervous system, Exp. Opin. in Drug Delivery, 5(2), 155-174, 2008.

G. Tosi et al., Glycopeptide-decorated nanoparticles as drug carriers for CNS: effects of surface coverage and carbohydrate type, J. Nanoneuroscience,1 (2),152-157, 2009.

B. Ruozi, et al, , Liposome-oligonucleotides interaction for in vitro uptake by COS I and HaCaT cells. J. Drug Target. 13 (5), 295-304, 2005.

B. Ruozi, et al, Dotap/Udca vesicles: novel approach in ODN delivery, Nanomedicine: Nanotechnology, Biology and Medicine, 3, 1-13, 2007.

B. Ruozi, et al., Flow cytometry and live confocal analysis for the evaluation of the uptake and intracellular distribution of FITC-ODN into HaCaT cells, J. Liposome Res. 19 (03), 241-251, 2009 .

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