

Advanced pharmaceutical technologies for antitumoral drug/gene targeting

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In our laboratory the delivery and targeting of antitumoral agents (drug, oligonucleotide, gene) to neoplastic tissues have been performed following two different strategies. In one approach, nonpolymeric nanoparticles or liposomes loaded with the drug have been prepared, either conventional or targeted. In the other approach, the drug is covalently bounded to a targeting moiety in order to modify its biodistribution and to improve its pharmacological proprieties.



1. Description of the product

Recently we have developed a revolutionary approach for the preparation of new non-polymeric nanoparticles for the delivery of drugs or small proteins. This approach is called “squalenisation of new materials” since it was used a natural unexpensive and non toxic material, squalene, widely known in cosmetics, to prepare nanoparticle linked to an active material (drug, or gene or protein). Squalene was chemically linked to an active product bearing a suitable functional group to give a squalenoyl prodrug that following Fessi procedure, in water, form very stable 100-200 nm nanoparticles, called squalene nanoparticles (SNP).

In the other approach (linking a drug to a targeting moiety), we prepared new cationic liposomes bearing an unexpensive targeting or bioadhesive material as hyaluronic acid (HA) to carry DNA or drugs for gene transfection or antitumoral activity.

2. Innovative aspects of the product

Squalene nanoparticles are stable as the polymeric one, but they are non toxic as solvent or tensioactive agent are not used for their preparation. Differently to classic polymeric nanoparticles, that usually show the same activity of the parent drug, these SNP seem to be more active and to have favourable pharmacokinetic properties.

Concerning the second approach, the new cationic lipids 2,3-didodecyl-oxy-propyl-dimethyl-hydroxy-ethyl bromide (DE), is associated with lipids such as DOPE or DPPE, linked to HA to give targeted cationic liposomes carrying DNA (gene or oligonucleotides) or drugs. We are able to select an appropriate HA (from 4.7 to 1500 KDa) to obtain bioadhesive or targeted liposomes usefull for ocular delivery or breast cancer.

3. Main advantages of the offer

SNP nanoparticles were first linked to gemcitabine as 4-(N)-squalenoylgemcitabine. We have evaluated in vitro the anticancer activity on cancer cell lines, in comparison to gemcitabine. The nanoassemblies were about 6- to 8-fold more cytotoxic than gemcitabine itself.

The cationic liposomes carrying HA and a reporter gene (luciferase) were non toxic and also two time more effective than the corresponding cationic liposomes without HA. So HA seems to potentiate the cationic liposomes (lipoplexes) transfection activity.

4. Technology keywords

Non polymeric nanoparticles, cationic liposomes, hyaluronic acid, Squalene, Gene transfection, antitumoral drugs

5. Current stage of development

Work in progress tested in laboratory

6. Intellectual property rights

NPS nanoparticles were covered by an international patent PCT /FR2005/050488. The intellectual properties rights were shared by L.Cattel group 33%, University of Torino and by P.Couvreur group, University Paris sud, France , 66%.

Technical and scientific publications

Immordino M.L., Brusa P., Rocco F., Arpicco S., Ceruti M., Cattel L. (2004) Preparation , charcterisation , cytotoxicity and pharmacokinetics of liposomes containing lipophilic gemcitabine prodrugs . Journal of Controlled Release 100: 331-346 . IP 3.297

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International Patent : B.Stella , F.Rocco , V.Rosilio, J.-M.Renoir , L.Cattel , P.Couvreur (2005) Nanoparticles from Gemcitabine derivates , PCT /FR2005/050488 . Now is going to be applied in Europe , USA , Canada , Japan , India and China .

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