

TECHNOLOGY PLATFORMS

Lipina™

Platform to produce drug delivery lipid colloidal carriers

Surf-Lipina™

Surface modification of Lipina™ for targeting or improvement of interaction of carriers with physiological membranes/environment

CATALIP

Lipid colloidal carriers for improved ocular drug delivery, longer persistency in conjunctival sac

NanodroM

Platform for micro emulsion as drug carriers, for different routes of administration

Microfluidic

Technology of microfluidic core-shell particles by incorporating drug candidates into different compartments of the particles



PATENTS

- Pharmaceutical compositions suitable for the treatment of ophthalmic diseases. Canada, patent no. 2,504,199 - WO2004/039351
- Pharmaceutical compositions suitable for the treatment of ophthalmic diseases. China, patent no. CN1756529
- Pharmaceutical compositions suitable for the treatment of ophthalmic diseases. India, patent no. 219920 - WO2004/039351
- Pharmaceutical compositions suitable for the treatment of ophthalmic diseases. EP, patent no. 1567125
- Pharmaceutical composition in form of solid lipidic microparticles suitable to parenteral administration, patent no. 6,238,694 WO98/56362.
- Solid lipidic nanospheres suitable to a fast internalization into cells , patent no. 6,685,960 WO00/30620
- Novel use of solid lipid nanoparticles comprising cholesteryl propionate and/or cholesteryl butyrate, patent no. 0001365626
- Formulations suitable to be administered transdermically containing active principles incorporated in sln, patent no. 0001375593 WO2008/041116



SCIENTIFIC PUBLICATIONS

- Peira E. et Al. -Transdermal permeation of apomorphine through hairless mouse skin from microemulsions. Int. J. Pharm. 226, 47-51 (2001)
- Priano L. et Al. - Controlled release transdermal Apomorphine treatment for motor fluctuations in Parkinson's disease Neurol Sci, Vol. 23, 99-100, 2002
- Priano L. et Al. Nocturnal anomalous movement reduction and sleep microstructure analysis in parkinsonian patients during one night Neurol Sci. 24(3), 207-8 (2003)
- Priano L. et Al. - Transdermal Apomorphine permeation from microemulsions: a new treatment in Parkinson's disease Movement Disorders, Vol. 19, No. 8, 937-942, 2004
- Bellò M. et Al. -Per technetate release from a water/oil microemulsion and an aqueous solution after subcutaneous inject in rabbits. Pharm Pharmacol. 46(6), 508-10 (1994 –June)
- Gasco MR et Al. - Long-acting delivery systems for peptides: reduced plasma testosterone levels in male rats after a single injection – IntJourPharmVol 62, Issues 2–3, 119-123,31 July 1990,
- Gasco MR et Al. - Microemulsions as topical delivery vehicles: ocular administration of Timolol- J Pharm Biomed Anal. 7(4), 433-9 (1989)
- Bargoni A. et Al. Solid Lipid Nanoparticles in Lymph and Plasma after duodenal administration to rats- Pharm.Res. 15, 745-750 (1998)
- Cavalli R. et Al. - Trans-mucosal transport of Tobramycin incorporated in SLN after duodenal administration torats. Part I- A Pharmacokinetic Study - Pharmacol. Res. 42, 541-545 (2000)
- Bargoni A. Et Al. - Transmucosal transport of tobramycin incorporated in solid lipid nanoparticles (sln) after duodenal administration to rats. Part II -Tissue distribution Pharmacol. Res., 43, 497-502 (2001)
- Zara G.P. et Al. - Pharmacokinetics and tissue distribution of Idarubicin-loaded Solid Lipid Nanoparticles after duodenal administration to rats. J. Pharm. Sci. 91, 1024-1033 (2002)
- Ugazio E. et Al. - Incorporation of cyclosporin A in solid lipid nanoparticles (SLN) - Int J Pharm., 241(2), 341-4 (2002)
- Cavalli R. et Al. - Duodenal administration of solid lipid nanoparticles loaded with different percentages of Tobramycin- J.Pharm.Sci. (2003)
- Cavalli R. et Al. - Evaporative drying of aqueous dispersions of Solid Lipid Nanoparticles -Drug Develop.Ind.Pharmacy. 27, 919-924 (2001)
- Marengo E. et Al. - Scale-up and intensification of an evaporative drying process applied to aqueous dispersions of solid lipidnanoparticles. Pharmac. Develop. Technol. 8, 299-309 (2003)



SCIENTIFIC PUBLICATIONS

MICROEMULSIONS – Transdermal administration

- Peira E. et Al. -Transdermal permeation of apomorphine through hairless mouse skin from microemulsions. Int. J. Pharm. 226, 47-51 (2001)
- Priano L. et Al. - Controlled release transdermal Apomorphine treatment for motor fluctuations in Parkinson's disease Neurol Sci, Vol. 23, 99-100, 2002
- Priano L. et Al. Nocturnal anomalous movement reduction and sleep microstructure analysis in parkinsonian patients during one night transdermal apomorphine treatment - Neurol Sci. 24(3), 207-8 (2003)
- Priano L. et Al. - Transdermal Apomorphine permeation from microemulsions: a new treatment in Parkinson's disease Movement Disorders, Vol. 19, No. 8, 937-942, 2004

MICROEMULSIONS – Subcutaneous Administration

- Bellò M. et Al. -Pertechnetate release from a water/oil microemulsion and an aqueous solution after subcutaneous inject in rabbits. Pharm Pharmacol. 46(6), 508-10 (1994 – June)
- Gasco MR et Al. - Long-acting delivery systems for peptides: reduced plasma testosterone levels in male rats after a single injection – IntJourPharmVol 62, Issues 2–3, 119-123, 31 July 1990,

MICROEMULSIONS - Ocular Administration

- Gasco MR et Al. - Microemulsions as topical delivery vehicles: ocular administration of Timolol - J Pharm Biomed Anal. 7(4), 433-9 (1989)

SLNs – Process Scale – Up

- Cavalli R. et Al. - Evaporative drying of aqueous dispersions of Solid Lipid Nanoparticles - Drug Develop.Ind.Pharmacy. 27, 919-924 (2001)
- Marengo E. et Al. - Scale-up and intensification of an evaporative drying process applied to aqueous dispersions of solid lipid nanoparticles. Pharmac. Develop. Technol. 8, 299-309 (2003)

SLNs – Reviews

- Gasco MR - Solid Lipid Nanoparticles from microemulsions- Pharm.Technol.Eur. 9, 52-58 (1997)
- Gasco MR - Solid Lipid Nanoparticles for Drug Delivery - Pharm.Technol.Eur. 13, 32-42 (2001)
- Priano L. et Al. - Transdermal treatment options for neurological disorders: impact on the elderly - Drug Aging 23(5), 357-75 (2006)
- Brioschi A. et Al. - Solid lipid nanoparticles: could they help to improve the efficacy of pharmacologic treatments for brain tumors? - Neurol Res. 2007 Apr; 29(3):324-30
- Gasco MR et Al. – Nanovector - Nanomedicine (Lond). 2007 Dec;2(6):955-60.
- Brioschi A. et Al. - Cholesterylbutyrate solid lipid nanoparticles as a butyric acid prodrug - Molecules. 2008 Feb 1;13(2):230-54.
- Gasco MR et Al. - Chapter 10 - Solid lipid nanoparticles and microemulsions for drug delivery The CNS. Prog Brain Res. 2009;180:181-92
- Brioschi A. et al - Chapter 11 - Solid lipid nanoparticles for brain tumors therapy: State of the art and novel challenges. - Prog Brain Res. 2009;180:193-223
- Gasco MR et al. – Chapter 13 - In Vivo Evaluations of Solid Lipid Nanoparticles and Microemulsions - DRUGS AND THE PHARMACEUTICAL SCIENCES, VOLUME 191, 219-238
- Musicanti C. et Al. - Solid Lipid Nanoparticles – SLN - Encyclopedia of Nanotechnology - 2012, pp 2471-2487

SLNs – Diagnostics

- Peira E. et Al. - In vitro and in vivo study of solid lipid nanoparticles loaded with superparamagnetic iron oxide J. Drug Target. 11 (1), 19-24, (2003)
- Morel S. Et Al. - NMR relaxometric investigations of solid lipid nanoparticles (SLN) containing gadolinium(III) complexes. Eur. J. Pharm. Biopharm. 45 (2), 157-163 (1998)
- Bello V. et Al. - Transmission electron microscopy of lipid vesicles for drug delivery: comparison between positive and negative staining - Microsc Microanal. 2010 Aug;16(4):456-61



SCIENTIFIC PUBLICATIONS

SLNs – Exvivo/ invitro studies - cell lines

- Pellizzaro C. et Al. - Cholesteryl butyrate in solid lipid nanospheres as an alternative approach for butyric acid delivery - *Anticancer Research*. 19, 3921-3926 (1999)
- Salomone B. et Al. - In vitro effects of cholesteryl butyrate solid lipid nanospheres as a butyric acid pro-drug on melanoma cells: evaluation of antiproliferative activity and apoptosis induction - *Clin.Exper.Metastasis* 18, 663-673 (2001)
- Ugazio E. et Al. - The effect of formulation and concentration of cholesteryl butyrate solid lipid nanospheres (SLN) on NIH-H460 cell proliferation - *Eur. J. Pharm. Biopharm.* 52, 197-202(2001)
- Guido M. et Al. - Growth inhibition of glioma cell lines by cholesteryl butyrate in solid lipid nanospheres - *Clin. Neuropathol.* 19, 151 (2000)
- Miglietta A. et Al. - Cellular uptake and cytotoxicity of solid lipid nanospheres (SLN) incorporating doxorubicin or paclitaxel - *Int.J.Pharm.* 210, 61-67 (2000)
- Mauro A. et Al. - Enhanced Cytotoxicity of Paclitaxel incorporated in Solid Lipid Nanoparticles against human glioma cells. - *Proc.Int. Symp.Control. Rel. Bioact. Mater.*, 27, 377-378 (2000)
- Brioschi A. et Al. - Confocal and electron microscopy of Solid Lipid Nanoparticles carrying Doxorubicin and colloidal Fe in glioma cell cultures - P 0-57 7th European Congress of Neuropathology, 13-16 July 2002, Helsinki (Finland)
- Mauro A. et Al. - Doxorubicin incorporated in Solid Lipid Nanoparticles: in vivo study in an animal model of cerebral glioma P-058 7th European Congress of Neuropathology, 13-16 July 2002, Helsinki, Finland
- Serpe L. et Al. - Cholesterol butyrate solid lipid nanoparticles as a butyric acid pro-drug: effects on cell proliferation, cell-cycle distribution and c-myc expression in human leukemic cells - *Anti-cancer Drugs*. 15(5), 525-36 (2004)
- Serpe L. et Al. - Cytotoxicity of anticancer drugs incorporated in solid lipid nanoparticles on HT-29 colorectal cancer cell line - *Eur. J. Pharm. Biopharm.* 58, 673-680, (2004)
- Serpe L. et Al. - Intracellular accumulation and cytotoxicity of doxorubicin with different pharmaceutical formulations in human cancer cell lines. - *J. Nanosci. Nanotechnol.* 6, 3062-9 (2006)
- Dianzani C. et Al. - Cholesteryl butyrate solid lipid nanoparticles inhibit adhesion of human neutrophils to endothelial cells- *Br J Pharmacol.* 148, 648-656 (2006)
- Zara G.P. et Al. - Effects of cholesteryl butyrate solid lipid nanoparticles in leukemia cell lines - *Pharm. Research* (submitted)
- Gobbi M. et Al. - Lipid-based nanoparticles with high binding affinity for amyloid-beta1-42 peptide.- *Biomaterials*. 2010 Sep;31(25):6519-29
- Serpe L. et al. - Solid lipid nanoparticles as anti-inflammatory drug delivery system in a human inflammatory bowel disease whole-blood model - *Eur J Pharm Sci.* 2010 Mar 18;39(5):428-36. Epub 2010 Feb 4
- Rivolta I. et Al. - Cellular uptake of coumarin-6 as a model drug loaded in solid lipid nanoparticles. - *J Physiol Pharmacol.* 2011 Feb;62(1):45-53
- Minelli R. et Al. - Cholesteryl butyrate solid lipid nanoparticles inhibit the adhesion and migration of colon cancer cells - *Br J Pharmacol.* 2011 Nov
- Minelli R. et Al. - Solid lipid nanoparticles of cholesteryl butyrate inhibit the proliferation of cancer cells in vitro and in vivo models. *Br J Pharmacol.* 2013 Sep;170(2):233-44
- Caretti A et Al. - Anti-inflammatory action of lipid nanocarrier-delivered myriocin: therapeutic potential in cystic fibrosis. *Biochim Biophys Acta.* 2014 Jan;1840(1):586-94
- ## **SLNs – Transdermal administration**
- Priano L. et Al. - Solid Lipid Nanoparticles Incorporating Melatonin as New Model for Sustained Oral and Transdermal Delivery Systems - *Journal of Nanoscience and Nanotechnology* Vol.7, 1–6, (2007)



SCIENTIFIC PUBLICATIONS

SLNs – Intravenous administration – Intraperitoneal administration

Bocca C. et Al. - Phagocytic uptake of fluorescent stealth and non-stealth solid lipid nanoparticles - Int. J.Pharm. 175, 185-193 (1998)

Zara GP et Al. - Pharmacokinetics of doxorubicin incorporated in solid lipid nanospheres (SLN) - Pharmacol Res. 40(3), 281-6 (1999)

Cavalli R. et Al. - Preparation and characterization of solid lipid nanospheres containing paclitaxel - Eur.J.Pharm.Sci. 10,305-309 (2000)

Podio V. et Al. - Biodistribution of Stealth and non-stealth solid lipid nanoparticles - J.Pharm.Pharmacol. 52,1057-1063 (2000)

Fundarò A. et Al. - Stealth and non-stealth solid Lipid Nanoparticles (SLN) carrying doxorubicin: Pharmacokinetics and tissue distribution after IV administration to rats - Pharmacolol. Res. 42, 337-343 (2000)

Zara G.P. et Al. - Intravenous administration to rabbits of non-stealth and stealth doxorubicin loaded solid lipid nanoparticles at increasing concentrations of stealth agent: pharmacokinetics and distribution of doxorubicin in brain and in other tissues - J. Drug Targeting 10, 327-335 (2002)

Brioschi A. Et Al. - Solid Lipid Nanoparticles Carrying Oligonucleotides Inhibit Vascular Endothelial Growth Factor Expression in Rat Glioma Models - J. Nanoneurosci. 1, 65–74 (2009)

Rezzani R Et Al. - Melatonin delivery in solid lipid nanoparticles: prevention of cyclosporine A induced cardiac damage - J Pineal Res. (2009)

Priano et.Al.- Baclofen-loaded solid lipid nanoparticles: Preparation, electrophysiological assessment of efficacy, pharmacokinetic and tissue distribution in rats after intraperitoneal administration. - Eur J Pharm Biopharm. 2011 Feb 23

SLNs – Oral/ /Duodenal administration

Bargoni A. et Al. Solid Lipid Nanoparticles in Lymph and Plasma after duodenal administration to rats - Pharm.Res. 15, 745-750 (1998)

Cavalli R. et Al. - Trans-mucosal transport of Tobramycin incorporated in SLN after duodenal administration torats. Part I - A Pharmacokinetic Study - Pharmacol. Res. 42, 541-545 (2000)

Bargoni A. Et Al. - Transmucosal transport of tobramycin incorporated in solid lipid nanoparticles (sln) after duodenal administration to rats. Part II -Tissue distribution - Pharmacol. Res., 43, 497-502 (2001)

Zara G.P. et Al. - Pharmacokinetics and tissue distribution of Idarubicin-loaded Solid Lipid Nanoparticles after duodenal administration to rats. J. Pharm. Sci. 91, 1024-1033 (2002)

Ugazio E. et Al. - Incorporation of cyclosporin A in solid lipid nanoparticles (SLN) - Int J Pharm., 241(2), 341-4 (2002)

Cavalli R. et Al. - Duodenal administration of solid lipid nanoparticles loaded with different percentages of Tobramycin - J.Pharm.Sci. (2003)

SLNs – Eye Topical administration

Cavalli R.et Al. - In vitro/in vivo evaluation of colloidallipospheres containing Pilocarpine as ion pair - Proceedings of the 1st World Meeting (APGI/APV,Budapest, Hungary, 1995, 801-802)

Cavalli R. et Al. - Solid lipid nanoparticles (SLN) as ocular delivery system for tobramycin - Int. J. Pharm. 238, 241-245 (2002)

Strettoi et Al - Inhibition of ceramide biosynthesis preserves photoreceptor structure and function in a mouse model of retinitis pigmentosa. -- -v Proc Natl Acad Sci U S A. 2010 Oct 26;107(43):18706-11

Piano I. et al - Cone survival and preservation of visual acuity in an animal model of retinal degeneration - EJM, Vol. 37, pp. 1853–1862, 2011

