1. FINAL PUBLISHABLE SUMMARY REPORT

Sonocaps - Ultrasonics synthesis of oil-filled proteins and polysaccharides microcapsules- was a two years (2009-2010) joint research project supported by the IRSES International Research Staff Exchange Funding Scheme. The partnership was composed of the Department of Chemical Science and Technologies, University of Rome (Italy), The School of Chemistry, University of Melbourne (AU), Department of Chemistry, University of Bath (UK). The University of Rome was responsible for the coordination of the project activities. Sonocaps was focused on the design of new, integrated microdevices (Figure 1) for imaging and controlled drug release.

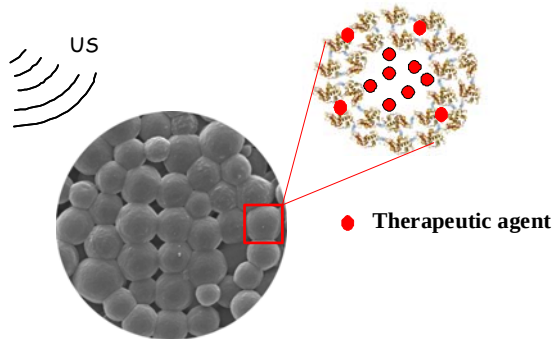
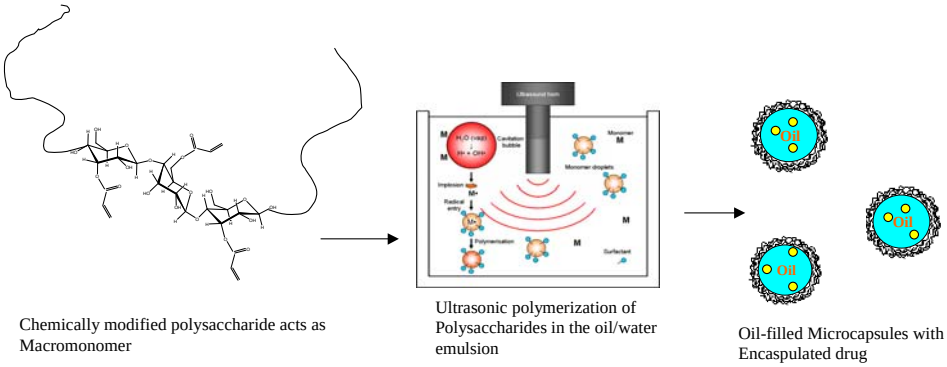


Figure 1: The design of ultrasound responsive microdevices for controlled drug delivery using sonochemistry

The fabrication of microcapsules made of polypetides, polysaccharides and biocompatible synthetic polymers raises a great interest in the biomaterials scenario. Such systems could solve problems associated with the delivery of conventional drugs and drug carriers, including poor site selectivity, polymer toxicity, non-biodegradability and free diffusion of drugs throughout the body. Achieving this goal has the potential to positively impact on the prevention, early diagnosis and "smart" treatment of diseases providing direct societal advantages.

The outcomes and achievements of scientific results in Sonocaps are briefly outlined:

1) Ultrasonic synthesis of oil-filled and air filled microcapsules using protein, polysaccharide and biocompatible synthetic polymers was successfully achieved. A schematic of the used technology is illustrated in Scheme1.



Scheme1. A schematic of the used technology

2) Structural and functional characterization of microcapsules properties were completed.

3) Ultrasonic encapsulation of ascorbic acid and doxorubicin into the core of the microcapsules was achieved and the stability and biological activity of encapsulated bioactive molecules were successfully evaluated.

4) Ultrasound triggered release of bioactive molecules and drugs from microcaspules was studied using model systems.

The success of Sonocaps has led to the publication of 3 papers in international journals and 3 papers submitted for publication to international journals in the area of Sonochemistry, Soft Matters and Biomedicine:

-Sonochemical Synthesis of Liquid-encapsulated Lysozyme Microspheres. Zhou M., Leong T.S.H, Melino S., **Cavalieri F**, Kentish S.,**Ashokkumar M** *Ultrasonics Sonochemistry* 2010Feb;17(2): 333-337.

-The Design of Multifunctional Microbubbles for Ultrasound Image-Guided Cancer Therapy **F. Cavalieri,** M. Zhou, **M.Ashokkumar** *Cur.Top in Med. Chem.*2010,12, , pp. 1198-1210(13).

-Tailoring the properties of ultrasonically synthesised microbubbles M. Zhou, F. Cavalieri and M. Ashokkumar *Soft Matter*, 2011, **DOI:** 10.1039/C0SM00652A

-One-Pot Ultrasonic Synthesis of Multifunctional Microbubbles and Microcapsules Using Synthetic Thiolated Macromolecules. **Cavalieri F**, Zhou M., Caruso F., **Ashokkumar M.,** Submitted to *Chem Comm* 2011.

-The modification of size and size distribution of ultrasonically synthesized microbubbles- Meifang Zhou, **Francesca Cavalieri and Muthupandian Ashokkumar**. submitted to Biomaterials 2011

-MOLECULAR PROPERTIES OF THE LYSOZYME- MICROBUBBLES: TOWARDS THE PROTEIN AND NUCLEIC ACID DELIVERY. **Sonia Melino,** Meifang Zhou, Mariarosaria Tortora, Maurizio Paci, **Francesca Cavalieri and Muthupandian Ashokkumar.** 2011 submitted to *Biomacromolecules.*

A number of invited talks and communications were presented at conferences: Biotechnology Australian Conference August 2009 Melbourne, Nanotech 2010 Venice Italy, FEBS 2010 Gothenburg Sweden, ICA 2010 Sydney, 1st Symposium on Interaction between Ultrasound and Microbubbbles, 9 January 2009, Nagoya, Japan, International Workshop on Advanced Materials for Australia's Future, 18-19 May 2009, Melbourne, Australia.

In addition to achieving scientific results in the ultrasonic synthesis of biocompatible microcapsules for delivery of therapeutic agents, the Sonocaps project also generated additional benefits for the partners in terms of transfer of knowledge and generated a basis for sustainable cooperation. Sonocaps allowed the strengthening of a research partnerships through exchanges of eight researchers and networking activities (seminars, conferences) between the University of Rome Tor Vergata, The University of Melbourne and the University of Bath. European and Australian researchers (academic staff and early stage researcher) have been introduced to the new technologies of ultrasonic synthesis of materials and biomaterials broadening their research and academic skills. The IRSES Mobility Programme provided support to the two European research organisations to establish and reinforce long-term research co-operation with Australia. Australian partner was supported by the Australian Academy of Science according the S&T agreement UE-AU. For continuing the collaborative research activities for a long-term the partnership put effort in applying, in the last two years, for Collaborative/STREP research projects within 7th Framework programme funding schemes:

- FP7-ICT-2010-C-FET-Open STREP proposal 256229 ,Sonotheri-II,
- HEALTH.2011.2.3.1-5: SME-targeted Collaborative Project- Small or medium-scale focused research project- TAMED

-NMP 2011.1.2-2 Large scale collaborative project- Nanocross.

In addition, a Memorandum of Understanding (5 years) between the University of Rome "Tor Vergata" and the University of Melbourne focused to the exchange of MSc and PhD students has been signed by the two educational Institutions.

Socio-economic impact of the overall project:

The long-term collaboration derived from Sonocaps benefits the institutions involved and the global community as a direct outcome of the research project in several biomedical applications.

The achievements of Sonocaps goals contribute to the European Research Policy objectives in the Nanotechnology and Information Society Technology areas. The project results provide fundamental

knowledge towards developing Nanomedicine as an “enabling technology”, which will help drive the EU to the forefront of this field. Nanomedicine aims to understand and exploit novel physical, chemical and biological properties of materials at the nanometre scale that can be utilised at the micro- and macro-scale for the mastering and processing of intelligent materials. The challenges for health represent an important priority within European policies. The whole philosophy of healthcare is to develop ways to deliver health services to patients as promptly and as locally as possible, which will require health practitioners to collaborate across disciplines and organisational boundaries. In this context, Sonocaps has contributed to the generation of an “intelligent environment” where an easy injection or implantation of “smart microbubbles or microcapsules” coupled with ultrasound or magnetic resonance imaging allow for the individualisation of disease prevention diagnosis and treatment. The development of innovative products and technologies, such as “drug-carrying targeted-microdevices”, could boost growth and the economic impact of biotechnology companies, especially SMEs, actively working on developing drug-delivery platforms, innovative diagnostics and imaging solutions. This is a niche where European Research can gain prestige and a corresponding share of the world market in the development, production and marketing of such “intelligent” devices. **Contact points**. Dr. Francesca Cavalieri, University of Rome Tor Vergata, francesca.cavalieri@uniroma2.it, Prof. Gareth Price, University of Bath, **g.j.price@bath.ac.uk,** Prof. Muthupandian Ashokkumar, University of Melbourne, **masho@unimelb.edu.au**