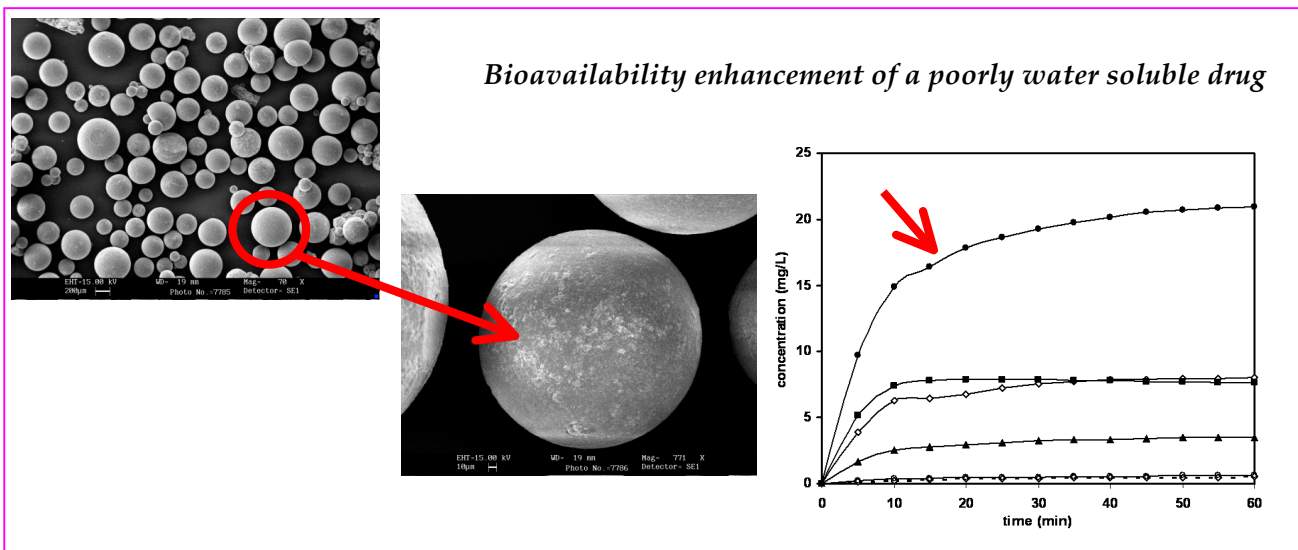


Solid Lipid Microparticles: formulation design and production technology

Dr Nadia Passerini, Dr Beatrice Albertini – University of Bologna – Consorzio TEFARCO Innova

Interest in Solid Lipid Microparticles (SLMs) is relatively recent and relates to the developments in the past ten years. Interest in this systems is largely driven by the fact that among Lipid Based Drug Delivery systems, SLMs well comply with the needs of the drug development process, as for instance safety, stability, different application's fields (pharmaceutical, veterinary, cosmetic as well as food additives) and administration pathways (oral, mucosal and topical delivery), ease of modifying the release of APIs, taste masking ability, rapidity and availability of several processing techniques. Moreover, advances in solvent free process technologies have greatly improved the potential for successful lipid based formulations without surfactants included. Actually the spray-congealing technique (alternatively called spray-chilling or spray cooling) is gaining considerable attention, especially from the view point of safety and of short time consuming. The spray-congealing technique atomizing a solution or a dispersion of the drug into a molten excipient overcomes the problem of residual solvents and the atomized droplets quickly solidify due to their exposure to an ambient air flow. The research in this field has developed two innovative atomizers for spray congealing: an ultrasonic atomizer and a two fluids nozzle called wide pneumatic nozzle (WPN).



1. Description of the product

SLMs are produced by spray congealing. One of the key elements of a spray congealing process is the atomization efficiency of the molten mixture that can be achieved through different types of atomizer. A recently developed device, called Wide Pneumatic Nozzle (WPN), is able to manage very viscous liquids and/or containing high amounts of solids (up to 50% w/w). The final particle size distribution is affected by formulation characteristics (viscosity, drug loading) and by processing parameters; in general dimensions can vary in the range 20 – 500 μm . This device also provided better performance than a conventional air pressure nozzle.

2. Innovative aspect of the product

In the last years the potential application of SLMs prepared by spray congealing for oral, topical and mucosal (buccal and vaginal) delivery was investigated.



i) A delivery system for Silybum Marianum dry extract with enhanced oral bioavailability by combining two technologies (mechanochemical activation and spray congealing) was produced. Microparticles containing the activated coground were produced by spray congealing technology using Gelucire 50/13 as a hydrophilic low m.p. carrier. Microparticles were spherical in shape, achieved satisfactory yield and high encapsulation efficiency. Moreover these microparticles demonstrated their ability to improve very significantly the oral bioavailability of the main flavolignans of Silybum Marianum dry extract in rats.

ii) A multi-composite wound dressing able to control the release of a water soluble API for several days was developed. The wound dressing was a microstructured spongy matrix, which embeds SLMs prepared by spray congealing. The characterization of the SLMs evidenced their spherical shape, mean dimensions lower than 20 μm , controlled release and the modification of the drug crystalline state. The final multi-composite platform was able to promote the growth of fibroblasts maintaining its prolonged release characteristic.

3. Main advantages of the offer

- The microencapsulation of drugs into low-melting materials is a practical and efficient one-step method that uses food grade and low cost excipients.
- The proposed technology is a solvent free and one step process.
- The SLMs may exhibit different size, potentially useful for various administration routes.

4. Technology key words

solid lipid microparticles - spray congealing – oral, topical and mucosal delivery.

5. Current Stage of Development

The equipment has been widely tested and is available and fully operational.

6. Intellectual Property Rights

The product is not covered by patent.

Technical and scientific publications

B. Albertini, N. Passerini, F. Pattarino, L. Rodriguez. New spray-congealing atomizer for the microencapsulation of highly concentrated solid and liquid substances. *Eur. J. Pharm. Biopharm.*, 2008, 69, 348-357.

B. Albertini, N. Passerini, M. Di Sabatino, B. Vitali, P. Brigidi, L. Rodriguez. Polymer-lipid based mucoadhesive microspheres prepared by spray congealing for the vaginal delivery of Econazole nitrate. *Eur. J. Pharm. Sci.* 2009, 36, 591-601.

N. Passerini, S. Qi, B. Albertini, M. Grassi, L. Rodriguez, DQM. Craig. Solid lipid microparticles produced by spray congealing: influence of the atomizer on microparticle characteristics and mathematical modeling of the drug release. *J. Pharm. Sci.* 2010, 99(2), 916-931.

B. Albertini, N. Passerini, M. Di Sabatino, D. Monti, S. Burgalassi, P. Chetoni, L. Rodriguez. Poloxamer 407 microspheres for orotransmucosal drug delivery. Part I: formulation, manufacturing and characterization. *Int. J. Pharm.* 2010, 399, 71-79.

N. Passerini, B. Perissutti, B. Albertini, E. Franceschinis, D. Lenaz, D. Hasa, I. Locatelli, D. Voinovich. A new approach to enhance oral bioavailability of Silybum Marianum dry extract: Association of mechanochemical activation and spray congealing. *Phytomedicine* 2012, 19, 160-168.

M. Di Sabatino, B. Albertini, V.L. Kett, N. Passerini. Spray congealed lipid microparticles with high protein loading: Preparation and solid state characterization. *Eur. J. Pharm. Sci.* 2012, 46, 346-356.

B. Albertini, M. Di Sabatino, N. Calonghi, L. Rodriguez, N. Passerini. Novel multifunctional platforms for potential treatment of cutaneous wound: Development and in vitro characterization. *Int. J. Pharm.* 2013, 440:238-49.

CONTACT

Consorzio TEFARCO Innova

c/o Dip.to di Farmacia, Viale delle Scienze 27/A, 43124 Parma - Italy

tefarco@nemo.unipr.it - Tel. 0521.905073 Fax. 0521.905006