

Newsletter

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14th Naples Workshop on Bioactive Peptides

14th Naples Workshop on Bioactive Peptides The 14th edition of the Naples Workshop on Bioactive Peptides will be held in Naples (Italy) at the *Centro Congressi* of the University of Naples *Federico II* from June 12th to 14th, 2014. The general subject selected for this 14th edition is "The Renaissance era of peptides in drug discovery". For more information, please visit: <http://www.14naplesworkshop.org>

The Renaissance era of Peptides in Drug Discovery



33rd European Peptide Symposium

The 33rd European Peptide Symposium (EPS) will be held at the National Palace of Culture, in Sofia (Bulgary), from August 31st to September 5th, 2014. This meeting will provide a great opportunity to exchange ideas and to create new collaborations between successful scientists working in the field of Chemistry, Biology and Pharmaceutical industry related to peptide science. For more information, visit: <http://www.33eps2014.com>.



20th International Symposium on Regulatory Peptides

Registrations for the 20th International Symposium on Regulatory Peptides (REGPEP 2014) are open. This meeting, which will be held in Kyoto, Japan, from 7th to 10th September, 2014, will cover topics such as identifying new peptides, interactions between ligands/receptors, the interaction of peptides with the blood-brain barrier, the effect of peptides on the brain, the cardiovascular system, gastrointestinal tract. The deadline for abstract submission is set to May 30th, 2014. For more program information, visit: www.regpep2014.com.



Conference

Dr **Michael CONLON** of the School of Biomedical Sciences, University of Ulster, Northern Ireland, will give a seminar entitled "The multi-faceted therapeutic potential of host-defense peptides from frog skin" at the University of Rouen, in the PRIMACEN meeting room (308) of the Main building of the Faculty of Science and Technology, on May 6th, 2014, at 11 AM.



PeReNE Steering Committee n°3

The third PeReNE Steering Committee took place in Portsmouth, on April 15th. Organised jointly by researchers of Portsmouth and Rouen, this meeting gathered around 40 participants involved in the PeReNE project. Four scientific presentations were given in the morning, including a presentation by Prof **Ijeoma UCHEGBU**, describing the activities of Nanomerics, a UK-based SME involved in nanoparticles and peptide delivery. During the afternoon the financial and administrative status of the project was addressed. Research teams also met to discuss ongoing research projects, and further collaborations. It was decided that the next PeReNE steering committee will be organised by **Michèle BOITEL**, **François GUÉRINEAU** and their colleagues at the Université de Picardie Jules Verne, Amiens, on October 26th and 27th 2014.





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The most common drug delivery route for proteins and peptides is currently the parenteral route, which is inconvenient and painful. Non-invasive delivery methods such as oral administration would be ideal, however proteins and peptides show a rather poor absorption from the gastrointestinal tract due to their large size and hydrophilicity;¹ moreover, even when peptides get into the bloodstream they often cannot reach their target organs in sufficient concentration. To circumvent these problems, encapsulation of peptides and proteins has become the focus of an alternative approach for developing novel drug delivery systems, which involves manufacturing nano-scale particles whose properties can be optimised depending on the desired mode of administration and target tissue.² Commonly used methods for protein/drug encapsulation in polymeric particles include solvent evaporation, spray drying, solid/oil/water emulsification, or coacervation; most of these methods expose peptides to various factors that can affect their stability such as organic solvents or high temperature, and polymer degradation may also promote deactivation during these processes.³ Electrospraying (using either single or coaxial systems, Figure 1) is an alternative technique that promises to overcome most of these limitations -as an emerging technology, electrohydrodynamic atomisation has a great potential for controlling the generation of nano scale morphologies and optimize their functionality.^{4,5}

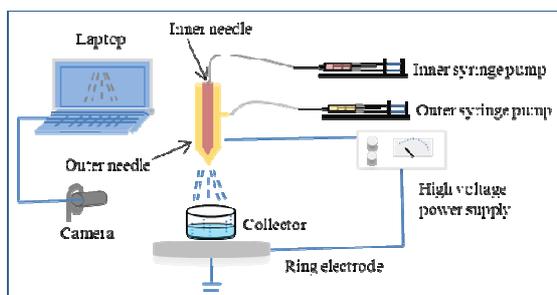


Figure 1. Experimental setup for an electrospraying system using single or coaxial needles for peptide encapsulation.

We are currently working on the encapsulation of octapeptide OP⁶ using single and coaxial electrospraying techniques. In a preliminary study, angiotensin II was employed as a model in order to evaluate the stability and degradation of short peptides exposed to high-voltage electric field. Both ELISA and HPLC analysis showed that angiotensin II stability was significantly affected only when very high voltage (30kV) and low flow rates (5µL) were applied (p=0.0015); interestingly, it was found that, for an applied voltage of 30 kV, there was no significant degradation when a higher flow rate was used.

An electrospraying single needle process was employed (flow rate 3µl/min and applied voltage 6-19kV) to generate the

nanoparticles containing the model peptide (angiotensin II) and modified chitosan (N-octyl-O-sulphate chitosan, NOSC).⁷

Loaded nanoparticles were analysed using Dynamic Light Scattering (DLS), Nanoparticle Tracking Analysis (NTA) and Scanning Electron Microscopy (SEM): following optimisation they were shown as spherical and with an average size of 60 nm (Figure 2a).

A further development of our electrospraying method employed a coaxial system where the peptide mixed with the modified polymer forms a core (inner layer) that is surrounded by a lipidic shell (outer layer). We believe this nano-construct allows for a more efficient encapsulation and increases the stability of the peptide drug, while also better controlling its release. Preliminary results showed particles of an average size of <100 nm when measured by DLS and NTA, and SEM images confirmed the spherical morphology and also the size of these nanoparticles (Figure 2b).

Further work will involve replacing the angiotensin II model peptide with the target octapeptide OP⁷ with the aim to produce "smart" nanocapsules for peptide delivery that can be tested in vivo.

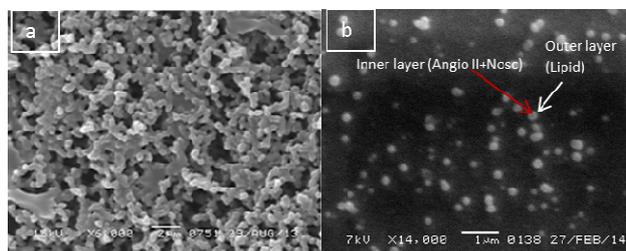


Figure 2. SEM images of: a) Angiotensin II loaded NOSC nanoparticles formed by single needle electrospraying, and b) lipid shell nanocapsules loaded with angiotensin II + NOSC.

References

- 1 Rao S.V.R., Agarwal P., Shao J., Self-nanoemulsifying drug delivery systems (SNEDDS) for oral delivery of proteins drugs: II. In vitro transport study. *Int. J. Pharm.* 2008; 362:10-15.
- 2 Cohen S., Yoshioka T., Lucarelli M., Hwang L.H., Langer R. Controlled delivery systems for proteins based on poly (lactic/glycolic acid) microspheres. *Pharm. Res.* 1991; 8:713-720.
- 3 Van de Weert M., Hoehstetler J., Hennink W. E. & Crommelin D. J. A. The effect of a water/organic solvent interface on the structural stability of lysozyme. *J. Control. Release.* 2000; 68:351-359.
- 4 Rasekh M., Ahmad Z., Day R., Wickham A., Edirisinghe M. (2011) Direct writing of polycaprolactone polymer for potential biomedical engineering applications. *Adv. Engin. Mat.* 2011; 13:B296-B305.
- 5 Ahmad Z., Nangrejo M., Rasekh M., Stride E., Edirisinghe M. Novel electrically driven direct-writing methods with managed control on in-situ shape and encapsulation polymer forming. *Int. J. Mat. Form.* 2013; 6:281-288.
- 6 Leprince J., Oulyadi H., Vaudry D., Masmoudi O., Gandolfo P., Patte C., Costentin J., Fauchère JL, Davoust D., Vaudry H., Tonon MC. Synthesis, conformational analysis and biological activity of cyclic analogs of the octadecanuropeptide ODN. Design of a potent endozepine antagonist. *Eur. J Biochem.* 2001; 268:6045-57.
- 7 Green S., Roldo M., Douroumis D., Bouropoulos N., Lamprou D., Fatouros DG. Chitosan derivatives alter release profiles of model compounds from calcium phosphate implants. *Carbohydr. Res.* 2009; 344:901-7.