A.It.U.N. 11th MEETING

Book of Abstracts

"Clinical experience and technological innovation in pain therapy: from traditional APIs to cannabinoids"

DATE:
11-12 MAY 2017

PALAZZO DEL MONTE DI PIETÀ
PADOVA

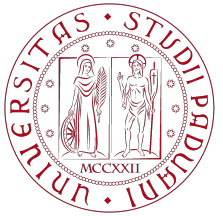
WWW.AITUN.IT
INFO@AITUN.IT

AAPS Italian University Network Student Chapter

dsf

Università degli Studi di Padova

Thanks to



UNIVERSITÀ
DEGLI STUDI
DI PADOVA

aaps®

American Association of
Pharmaceutical Scientists

And thanks to Fondazione Cassa di Risparmio di Padova e Rovigo for the concession of the conference room at Palazzo del Monte di Pietà.

PROGRAM PLANNING COMMITTEE

Francesca Borgna, MS – University of Padova

Serena Bertoni, MS - University of Bologna

Laura Tiozzo Fasiolo, MS - University of Parma

Silvia Pisani, MS – University of Pavia

Elisa Gurian, MS – University of Trieste

FACULTY ADVISOR

Prof. Nicola Realdon - University of Padova

LOCAL ORGANIZING COMMITTEE

Roberto Baggio, Elisa Vettorato, Martina De Santi, Marta Pellizzola, Chiara Favaretto, Sara Bettonte, Mattia Berton, Martina Marcon, Elena Prisco, Valentina Cicolin, Gianandrea Quaggiotto

MEETING PROGRAM

11th MAY - PALAZZO DEL MONTE DI PIETÀ

12.00 - 13.30	Participants registration
14.00 - 14.30	Meeting inauguration *Francesca Borgna* *Prof. Nicola Realdon*

1st afternoon session
Chairs: Francesca Borgna, Serena Bertoni

14.30 – 15.25	Pain physiopathology *Prof. Francesco Ambrosio*
15.30 – 16.00	Treatment of neuropathic pain *Prof. Maurizio Evangelista*

Coffee break

2nd afternoon session
Chairs: Laura Tiozzo Fasiolo, Elisa Vettorato

16.30 – 17.00	Treatment of nociceptive pain *Prof. Pietro Giusti*
17.00 – 17.30	Transdermal delivery of pain killers: advantages and limitations *Prof. Patrizia Santi*
17.30 – 18.00	Nanofibrillar cellulose membrane; - new promising candidate for wound healing treatment *Prof. Marjo L Yliperttula*
From 20.00 on	Social Dinner Event at Caffè Pedrocchi

12th MAY - PALAZZO DEL MONTE DI PIETÀ

1st morning session
Chairs: Elisa Gurian

09.30 – 10.00 The use of ceramic materials for an abuse deterrent transdermal fentanyl patch
Dr. Ulrika Espefält Westin

10.00 – 10.30 New diagnostic and therapeutic approaches for autoimmune diseases
Dr. Paolo Macor

Coffee break

2nd morning session
Chairs: Silvia Pisani

11.00 – 11.20 On the characterization of SEBS pressure sensitive adhesives for the design of cutaneous patches
Gaia M.G. Quaroni

11.20 – 11.40 Silk fibroin nanoparticles dramatically reduce celecoxib in vitro cytotoxicity
Barbara Crivelli

11.40 – 12.00 Nasal region as an appealing route for brain delivery of nanoencapsulated statins
Adryana Rocha Clementino

12.00 - 14.30 Light Lunch and Poster session

Afternoon session

Chairs: Serena Bertoni, Roberto Baggio

14.30 – 15.00	P4 effects of a standardized extract of non psychotropic *Cannabis sativa* L. on central and peripheral inflammatory responses *Vittoria Borgonetti*
15.00 – 15.30	N-acyl ethanolamines in the treatment of abnormal pain: new mechanism of action of the N-palmitoylethanolamide *Dr. Livio Luongo*
15.30 – 15.50	Micro-RNA nanoparticles for gene silencing: measuring size and zeta potential with light scattering technology *Laura Graziano - Anton Paar*
15.50 – 16.20	Clinical use of Cannabis: national and regional regulatory issues *Dr. Umberto Gallo*
16.20 – 16.40	Synthesis and purification of desoxy-CBD precursors for innovative pain therapy formulations *Elisa Vettorato*
16.40 – 17.00	Poster awards XII A.It.U.N. Meeting Early Announcement Final remarks

MAIN LECTURES

PAIN PHYSIOPATHOLOGY

Francesco Ambrosio

Department of Medicine, University of Padova

Acute pain is essential to survive and represents a warning signal of tissue damage that keeps the organism on the lookout for anything that could cause additional damage.
The physiology of the nociceptive event starts from the activation of sensory receptors (nociceptors) which form the first neuron (Aδ, C fibers); after passing through the dorsal root of spinal nerve, the signal reaches the second and thereafter the third neuron. This process originates what is clinically defined as "nociceptive pain": a kind of pain generated by an ordinary nerve that communicates the information of tissue damage to the central nervous system.
There is a different type of pain, called "neuropathic pain", recently defined as a pain directly caused by lesion or disease of the somatosensory system.
Chronic pain, on the other hand, does not keep a "warning" function and furthermore debilitates the patient through sleep disorders, anorexia, letargia, personality crysis, depression: a scenery that corresponds with the depletion of adaptive response. Chronic pain is not only a peripheral event: it is a disease characterized by the symptoms which comes with it.
Clinical situations that show chronic inflammation (like rheumatoid arthritis or cancer) present a high prevalence of comorbidity of depression and pain, suggesting the presence of common mechanisms. Neuroimmune mechanisms, which interlink the immune system with the central nervous system, are probably involved in the pathogenesis of both chronic pain and depression. The common mechanism that is likely to connect these two clinical situations is the inflammation, the biochemical event that represents an adaptative response caused by specific conditions like infections, tissue damage or nociceptive stimuli and that aims to restore tissue structure and function.

*Prof. **Francesco Ambrosio** graduated in Medicine at the University of Padua in 1974. He then completed his studies with the specialization in Anesthesiology at the same University where he is now Associate Professor. He is also director of the "Servizio Aggregato di Terapia Antalgica dell'Istituto di Anestesia e rianimazione".*

TREATMENT OF NEUROPATHIC PAIN

Maurizio Evangelista

Istituto di Anestesiologia, Rianimazione e Terapia del Dolore, Università Cattolica del Sacro Cuore, Rome

Neuropathic pain (IASP definition: pain caused by lesion or disease of the somatosensory nervous system) represents a type of cronic non-oncologic pain where the pain is no longer a symptom with protective features, but rather a hardly reversible maladaptive situation (disease); at the same time, it represents one of the most complex clinical pictures in terms of the development of an effective and sustainable therapy.

From the clinical point of view, this leads to a variable percentage of patients, ranging from 35 to 50%, with a poor quality of life due to the inability of achieving an adequate relief from pain.

Numerous contributions to the scientific international literature, apart form providing documentary evidence of a biopsychosocial impact greater than the one that derives from cardiovascular and metabolic diseases, highlight the need to modify the therapeutic approach, directing it towards a semeiotic criterion (pain phenotype: specific signs and symptoms of a certain type of neuropatic pain in a specific moment), which is an epiphenomenon of underlying pathogenetic mechanisms, instead of basing it on a etiologic criterion.

This would enable a more appropriate prescription and greater efficiency, taking into primary consideration the possibility of getting back to everyday life rather than obtaining complete analgesia.

A therapeutic protocol should be, especially in case of cronic pain, effective as well as sustainable in terms of both biologic aspect (effectiveness/safety ratio) and acceptability (minimum interference with professional, relational and social life). All the above-mentioned aspects are equally important but one of them can prevail over the others depending on the patient characteristics and background.

From that derives the concept of personalized "dynamic" therapy, where the doctor, once identified the realistic objectives that the patient wants to achieve, has to define the best possible protocol basing on his expertise and on the available treatments, as well as periodically re-evaluate the clinical trend in order to provide modifications or integrations to the therapy, if necessary.

The present contribution aims to:

• Describe the State of the Art in pathogenetic mechanisms and relate them to

the signs and symptoms of neuropathic pain

• Present the pain phenotype as a mean of dynamic "profiling" on the basis of which it is possible to prescribe a therapeutic regimen appropriate for every stage of the clinical picture.

• Describe the currently available drugs in basis of a "mechanism oriented" criterion

• Present the methods of titration, monitoring and tapering of medications with respect to variations of the patient conditions.

Prof. ***Maurizio Evangelista*** *is Director of the operating unit for Pain therapy at the Università Cattolica del Sacro Cuore (Rome, Italy), where he has been a professor at the Advanced School in Anesthesiology and Reanimation since 1998. He is professor of physiopathology and Pain Therapy at the University of Cagliari, University of Padova and Università Cattolica del Sacro Cuore (Rome, Italy) and his didactic activity extended also to the University of Tor Vergata (Rome, Italy) and to the University of L'Aquila (Italy).*

TREATMENT OF NOCICEPTIVE PAIN

Pietro Giusti

Department of Pharmaceutical and Pharmacological Sciences, University of Padova

Analgesics or painkillers comprise a group of drugs used to provide relief from nociceptive pain. Analgesic drugs act in different ways on the peripheral and central nervous systems. They are distinct from anesthetics, which temporarily affect or eliminate sensation. Analgesics include paracetamol, the non-steroidal anti-inflammatory drugs (NSAIDs) and opioids. When choosing analgesics, the severity and response to other medication determines the choice of agent; the World Health Organization pain ladder specifies mild analgesics (i.e. NSAIDs) as its first line. Analgesic choice is also determined by the type of pain: e.g., for neuropathic pain, the above types of analgesics are less effective, and benefit may often be achieved using classes of drugs are not normally considered analgesics, such as tricyclic antidepressants and anticonvulsants.

My presentation will discuss mainly opiate analgesics. The recent finding, at Sumerian city of Uruk, of clay tablets describing opioid therapeutic properties dates back about 7,000 years and clearly shows that opioid analgesics, despite their many drawbacks, have always been considered the most potent analgesics known for acute (perioperative) and chronic pharmacological treatment. However, opioid use carries with it the potential for serious adverse effects: respiratory depression, abuse development, and addiction / death from accidental overdose. The incidence of these effects has increased considerably in recent decades, mainly because prescriptions of these drugs have experienced a significant expansion [Kharash, 2016]. This phenomenon is partly attributed to increased awareness by clinicians for the diagnosis and treatment of pain, but also to pressure exerted by the pharmaceutical industry to promote opioids use for the treatment of moderate to severe pain [Okie, 2010].

Emerging data suggests that in a not too distant future, we will have new analgesic molecules capable of producing long-term naloxone-reversible pain relieve via the opioid system. Furthermore, these molecules seem to cause less respiratory depression than commonly used opioids (such as morphine) when combined with a lesser abuse potential. These new possibility will be discussed.

Prof. ***Pietro Giusti*** *has graduated in Medicine and Surgery in University of Padua in 1975. His didactic and research activity started in 1978 working at the University of Padua, Bologna, and Ancona. He became full professor of Neuropsychopharmacology in 2004 at the University of Padua where he has been director of the Specialization School in Medical Toxicology since 2003. He has been visiting professor of Pharmacology at the Georgetown University - Pharmacology Department in 1989-1990 (Washington D. C., USA) and in 1995 he spent a period at the Allegheny Singer Research Institute- Medical College of Pennsylvania - Psychiatry Department (Pittsburgh, U.S.A).*

TRANSDERMAL DELIVERY OF PAINKILLERS: ADVANTAGES AND LIMITATIONS

Patrizia Santi

Food and Drug Department,
University of Parma

Transdermal delivery of painkillers has a long history, starting with hot chili and methyl salicylate plasters. Today, NSAIDs, opioids (fentanyl and buprenorphine) and local anesthetic (lidocaine) patches are available. This presentation will focus primarily on opioid transdermal delivery systems.

The efficacy of transdermal fentanyl for cancer pain and chronic non-cancer pain (chronic lower back pain, rheumatoid arthritis, osteoarthritis, neuropathic pain) is well established. A meta-analysis of three randomized clinical trials comparing slow release oral morphine with transdermal opioids in patients with moderate-severe cancer pain revealed a statistically significant reduction of the incidence of constipation with transdermal therapy, with no difference in overall side effects. Other clinically relevant benefits include ease of use, less interference with normal course of daily life, improved compliance and bypass of first pass metabolism.

From the first introduction into the market, several formulations of fentanyl transdermal systems have been developed to improve drug delivery and prevent misuse of the active principle. Liquid reservoir systems, the first used, had safety liabilities linked to the risk of leakage of the liquid drug reservoir and substance abuse issues, due to the ease of extracting the liquid formulation. Modern matrix-based systems, containing the active dispersed or dissolved in a polymeric matrix, have largely overcome these limitations.

Several formulations of fentanyl transdermal systems have been developed to improve the drug delivery and prevent misuse of the active principle.

With the aim of improving drug delivery, an iontophoresis system (IONSYS®) was approved in the US, only for hospital use. The same device was initially approved also by EMA, but is no longer authorized from 2009 for quality related issues. Iontophoresis has been successfully applied also to the local delivery of local anesthetic, such as lidocaine: the device, Iontocaine®, was approved in 1995 in the US but was discontinued by the producer in 2004.

Despite all these efforts, the extent of patch use is still limited. In a recent survey on the use of opioids for the management of chronic pain among primary care physicians, orthopedists, rheumatologists and pain management specialists. The outcome of the survey revealed that, concerning the administration route, approx.. 15% of the patients were treated with

transdermal opioids, whereas approx.. 50% received oral medications. Interestingly, pain management specialists where the ones more active using the transdermal route (17%).

Dr. ***Patrizia Santi*** *received her Pharm. D. in 1987 and Ph.D. in Pharmaceutical Chemistry and Technology in 1992, from the University of Parma (Italy), where, from 1991 to 1998, she was Assistant Professor. From 1998 to 2002 she was Associate Professor of Pharmaceutical Technology at the Faculty of Pharmacy of the University of Parma (I), where she holds a position of Full Professor of Pharmaceutical Technology from 2002. From November 2008 to July 2012 she was director of undergraduate studies in Chemistry and Pharmaceutical Technology. From July 2012 to December 2017 she was Chair of the Department of Pharmacy, University of Parma.*

NANOFIBRILLAR CELLULOSE MEMBRANE; - NEW PROMISING CANDIDATE FOR WOUND HEALING TREATMENT

T. Hakkarainen[1,4], R. Koivuniemi[1], C. Escobedo-Lucea[1,2], A. Sanz-Garcia [1,2,3], J. Vuola[4], J. Valtonen[1,4], H. Kavola[4*] and M. Yliperttula[1*]

[1]Faculty of Pharmacy, Division of Pharmaceutical Biosciences, CDR, Academy of Finland, University of Helsinki, Helsinki, FINLAND; [2]Institute of Advanced Biomedical Engineering, Tokyo Womens Medical University (TWINS), Tokyo, JAPAN; [3]Ciberer, Valencia, SPAIN; [4]Helsinki University Hospital

Introduction: The most significant cause is the thermal injury, which accounts 6.3 million cases per year, some of them really severe and also including 19500 deaths caused by fired induced burns (http://www.who.int). Other causes of skin loss include trauma, diabetic ulcers, pressure and venous stasis. Wound care consumes a substantial proportion of the healthcare budget of western countries (Franks and Flanagan, Ewma council, 2006). The World Health Organization (WHO) has realized about the urgency of prevention and treatment; for that reason, it has developed a 10 year plan since 2008 to fight against burn wound healing. During the last two decades, extraordinary advances in cellular and molecular biology have greatly expanded the knowledge about the processes involved in acute-wound healing (Mustoe, 2004) and the arising of possible treatments, but "while 80% of US and Japan hospitals are using advanced methods, 80% of the Europeans continue using traditional therapies" Professor Peter Vowden said in an interview in 2007. European community has a special call under FP7 framework health program, for funding wound healing research.

Motivation: Wound and burns care patients have a high risk for infection due to damage to the skin barrier function. Infection may lead to chronic inflammation that often results in delayed wound healing, higher mortality, and higher costs due to longer hospitalizations.

The aim of this project is to develop nanofibrillar cellulose (NFC) material based treatments for wound and burns care purposes. During the project, the physical and chemical characteristics of NFC membrane will be optimized. Materials and methods: During the study the NFC membranes are tested with about 20 patients at the in skin graft donor site treatment in Helsinki Burn Centre. Based on the first in vivo clinical studies (patients 1-6) with NFC membrane in skin graft donor site treatment among burn patients, the modifications of the physical properties of the NFC membrane were performed. Comparisons between the NFC membranes and Suprathel® are

carried out by the treatments of patients 5-20.
Results: Based on the clinical tests the elasticity, amount of NFC at membranes and the physical size of the membranes used for the treatments were optimized. The optimized NFC membrane detached by itself in dry form in most cases at the 17th post operative date, and the skin donor site was recovered at least as well as the Suprathel®.
Conclusions: Based on the in vivo clinical data the NFC membrane seems to be very promising in skin graft donor site treatment, since it attaches to wound bottom, remains in place until skin graft donor site has healed. In some cases the NFC membrane operated even better than the control material Suprathel®. Therefore NFC membrane seems to be very promising in skin graft donor site treatment, but still some improvements have to been made and are under developemnt.

Acknowledgments: Academy of Finland, projects Finskin, Vaturp and mobility grants; Tekes of Finland, UPM.

Dr. ***Marjo Yliperttula*** *received her Ph.D. in Chemistry in 1993 (University of Helsinki, Finland). She served as Group Manager of Physical Chemistry, PK Simulations, and Early ADME at Orion Pharma. She has also served as Professor and Head of Division of Biopharmaceutics and Pharmacokinetics at the University of Helsinki, Faculty of Pharmacy. She has obtained international research experience as a post-doctoral fellow (Centre d'Etudes de Atomique Moleculaire, Saclay, France) and visiting professor (Riga Technical University, University of Padova, and Harvard Medical School). Dr. Yliperttula recently joined CDR at the University of Helsinki.*

THE USE OF CERAMIC MATERIALS FOR AN ABUSE DETERRENT TRANSDERMAL FENTANYL PATCH

Ulrika Espefält Westin

Emplicure AB

Cancer patients often need around-the-clock opioid treatment for moderate to severe pain. Fentanyl transdermal patches replaced every 72 hours are commonly prescribed. Unfortunately, abuse and misuse of these patches is an increasing problem, especially in the USA. The routes of abuse are primarily by oral ingestion, inhalation, smoking and injection after dissolution of the patch. As these patches need to contain a large dose of fentanyl for correct drug delivery to the body, abuse and misuse can be lethal.

The Food and Drug Administration in the USA are therefore encouraging the development of opioid formulations with abuse-deterrent properties to help combat the opioid epidemic.

One of the challenges in developing abuse deterrent formulations is that the patient does not gain remarkable benefits. The new products need to be bioequivalent to the ones on the market, but demonstrate abuse deterrent properties to decrease the risk to the public health.

Abuse deterrent properties can for example be achieved using physical/chemical barriers, agonist/antagonist combinations, aversion agents and delivery systems[1].

Emplicure AB combines physical/chemical barriers in a patented drug delivery system. The main barrier is the ceramic material used, geopolymers. Geopolymers are referred to as inorganic polymers or alkali-bonded ceramics. Geopolymers are formed by a reaction between aluminosilicate and an aqueous alkali solution (metakaolin and waterglass), molded and cured. By varying the composition and synthesis conditions, geopolymers can exhibit various physical and chemical properties.

Emplicure AB is developing an abuse deterrent transdermal patch where fentanyl is incorporated in geopolymer particles with high mechanical strength, which are then integrated in the adhesive of the patch. A prototype patch has demonstrated abuse deterrent properties in comparison to one product on the market. The prototype patch showed promising results for resistance against heat and extraction in different solvents like low pH and 40% ethanol[2].

[1]FDA Guidance for Industry Abuse-Deterrent Opioids — Evaluation and Labeling

[2]Bing Cai, Håkan Engqvist and Susanne Bredenberg Development and evaluation of a tampering resistant transdermal fentanyl patch Int J Pharm 488 (2015) 102 - 107

Dr. ***Ulrika Espefält Westin*** *holds a MSc Pharm and PhD in Pharmacy from Uppsala University. She defended her thesis with the title "Olfactory Transfer of Analgesic Drugs After Nasal Administration" in 2007. She has gained different working experiences in many pharmaceutical companies and in several different positions. From 1998 to 2001 she worked in AstraZeneca, Sweden, as Quality Engineer and GMP Training Coordinator. After receiving her PhD in 2007, she worked for Orexo, Sweden, when she held the positions of Quality Manager, Product Developer and Process Developer. From 2012 to 2016 she covered the position of Senior Formulation Scientist and Tech Transfer Project Manager at Kemwell, Sweden. Ulrika is currently responsible for the management of the project activities (Project Manager) at Emplicure AB, Sweden.*

Targeted approaches for the treatment of rheumatic diseases

Paolo Macor

Life Sciences Department, University of Trieste

Rheumatic diseases is a group of conditions characterized by inflammation of different tissues and causing intermittent, often chronic pain. Disease-modifying antirheumatic drugs remain the main desired strategy for their treatment. In particular, for rheumatoid arthritis patients, Methotrexate (MTX) is still the "anchor" drug but many patients treated for long term showed reduced efficacy and several side effects. Biological response modifiers, such as monoclonal antibodies able to block cytokines, are now the most successful drugs used to treat rheumatic diseases. However, despite these advances in medical treatment over recent years, many patients fail to respond to these therapies.

In this scenario, new therapeutic approaches are needed in order to guarantee increased efficacy while avoiding side effects. The selective delivery of drugs or recombinant antibodies to inflamed micro-environment represents a potential strategy to obtain the desired results. These may include new recombinant antibodies or targeted nanoparticles.

*Prof. **Paolo Macor** is a researcher since 2010 and professor of Molecular Immunology since 2012 at the University of Trieste; he is also scientific vice-director of Fondazione Callerio ONLUS since 2014. Paolo Macor has a degree in Medical Biotechnology and a degree in Biomedical Lab Technician obtained at the Faculty of Medicine of the University of Trieste. Among his research experiences, he had been Senior Researcher at ADIENNE Pharma and Biotech for more than 2 years. More recently he was trained as Entrepreneurs in Clinical Academia, initiative from the Federation of Clinical Immunology Societies (FOCIS), supported by Cellgene and delivered by INSEAD: Business School for the World (Fontainebleu, France).*

EFFECTS OF A STANDARDIZED EXCTRACT OF NON PSYCHOTROPIC *CANNABIS SATIVA* L. ON CENTRAL AND PERIPHERAL INFLAMMATORY RESPONSE

Vittoria Borgonetti, Paolo Governa, Silvia Galatello, Marco Biagi and Elisabetta Miraldi

[1]*Università degli Studi di Siena, Dipartimento di Scienze Fisiche, della Terra e dell'Ambiente.*
borgonetti@student.unisi.it

Introduction. Phytocannabinoids are cannabinoids that occur naturally in the cannabis plant.
Literature focused on cannabidiol (CBD), a major non-psychotropic constituent of cannabis; which shows diverse biological activities, particularly as an anti-inflammatory agent. In addition, *Cannabis sativa* L. contains terpenoids and flavonoids. The potential synergism of these components indicates that the whole phytocomplex can more effectively act as a drug with respect to the individual components.
The principal aim of this work was to generate an inflammation model, able to stimulate and activate both microglial and peripheral mononuclear cells as well as to modulate CBr expression, in order to evaluate the effects of a non-psychotropic extract of *Cannabis sativa* L. (EXT) and its major constituent, cannabidiol (CBD) and -caryophillene (CAR), on central neuro-inflammation and on peripheral inflammation.
Methods. Two cell lines were used: a mouse microglial cell lines (BV2) and peripheral blood mononuclear cells (PBMC); effects on neuro- and systemic inflammation were evaluated, respectively.
Results. A central and peripheral acute inflammation model with a brief (2 hours) LPS 250 ng/ml stimulation on BV2 and PBMC has been produced, obtaining the following results: substantial production of TNF-, IL-6 and IL-1; maximum modulation of CB1 and CB2 mRNA expression; no substantial variation in cell viability and slight morphological changes. To evaluate the anti-inflammatory effect mediated by EXT and its main components, we have focused the attention on influence of EXT, CBD and CAR on CB1 and CB2 mRNA expression and inhibition of cytokines production in basal condition and in acute inflammatory model. The results showed that EXT wasn't able to revert the effect of LPS on CB1 and CB2 mRNA expression in BV2, at the same time inhibiting cytokines production. On the contrary, EXT has no effect on cytokines production in PBMC, but contrasts mRNA down-regulation induced by LPS stimulation. In summary, EXT seems to act similarly to its major

components, regarding CBr modulation. Nevertheless, this action is not related to the final effect on cytokines inhibition, acting as a classic anti-inflammatory agent. EXT activity, then, does not directly rely on CBr modulation, which seems to be related to other intracellular pathways involved in inflammatory process. Indeed, CBr modulation could be affected by the activation of rapid intracellular responses to inflammation, such as NF-κB phosphorylation. Given this hypotheses, preliminary data on this key pathway have been obtained through immunofluorescence: NF-κB translocation, in fact, was observed yet after 30 minutes of LPS 250 ng/ml stimulation, with a maximum peak after 1 hour, both in BV2 and PBMC. EXT, similarly to CBD and CAR, reduced NF-κB translocation after 1 hour of LPS stimulation, suggesting this as a potential mechanism of action.
Conclusion. Cannabis anti-inflammatory activity seems to be related to classic intracellular pathways; CBr-based mechanism of action, however, are worth to be deeply investigated. Cannabis phytocomplex synergism, moreover, involves a moderate antioxidant activity. The synergism between hemp anti-inflammatory and anti-oxidant activity represents an interesting therapeutic approach for the management of neuro-inflammation and neurodegenerative diseases.

*Miss **Vittoria Borgonetti** is a young doctor graduated with final grade 110/110 in Pharmacy and Industrial Pharmacy at the University of Siena, Department of Biotechnology, Chemistry and Pharmacy.*
For her Master thesis she worked on the project "Effects of a standardized extract of non psychotropic Cannabis sativa L. on central and peripheral inflammatory response." Last year (December 2016), she attended the 4th SYRP Congress in Padua presenting the "Effects of a standardized extract of non psychotropic Cannabis sativa L. on central and peripheral inflammatory response".

N-ACYL ETHANOLAMINES IN THE TREATMENT OF ABNORMAL PAIN: NEW MECHANISM OF ACTION OF THE N-PALMITOYLETHANOLAMIDE

Livio Luongo and Sabatino Maione

Department of Experimental Medicine, Division of Pharmacology, University of Campania, Naples

The endogenous fatty acid amide palmitoylethanolamide (PEA) has been shown to exert anti-inflammatory actions mainly through inhibition of the release of pro-inflammatory molecules from mast cells, monocytes and macrophages. Indirect activation of the endocannabinoid (eCB) system is among the several mechanisms of action that have been proposed to underlie the different effects of PEA in vivo. In this study, we used cultured rat microglia and human macrophages to evaluate whether PEA affects eCB signaling. PEA was found to increase CB2 mRNA and protein expression through peroxisome proliferator-activated receptor-α (PPAR-α) activation. This novel gene regulation mechanism was demonstrated through: (i) pharmacological PPAR-α manipulation, (ii) PPAR-α mRNA silencing, (iii) chromatin immunoprecipitation. Moreover, exposure to PEA induced morphological changes associated with a reactive microglial phenotype, including increased phagocytosis and migratory activity. Our findings suggest indirect regulation of microglial CB2R expression as a new possible mechanism underlying the effects of PEA. PEA can be explored as a useful tool for preventing/treating the symptoms associated with neuroinflammation in CNS disorders.

*Dr. **Livio Luongo** graduated in Pharmacy at the University of Naples Federico II and received his Ph.D. in Pharmacology in 2008 from the Second University of Naples (Italy) where he obtained a post-doctoral fellowship in Neuropharmacology, in collaboration with the William Harvey Research Institute (Queen Mary University, London, UK) until 2012. During his Ph.D., he spent two years at the "Wolfson CARD" King's College in London.*
Currently, he works as researcher at the Second University of Naples in the Department of Experimental Medicine – Division of Pharmacology.

MICRO-RNA NANOPARTICLES FOR GENE SILENCING: MEASURING SIZE AND ZETA POTENTIAL WITH LIGHT SCATTERING TECHNOLOGY

Laura Graziano

Anton Paar

RNA interference is a highly promising gene silencing technique in which translation of the target gene's messenger RNA (mRNA) is inhibited by short complementary RNA sequences. These include the so-called small interfering-RNAs (siRNA), which are double-stranded and whose sequence is perfectly complementary to that of the target mRNA, therefore acting with a high degree of specificity, and the single-stranded micro-RNAs (miRNA), which can interfere with a broader range of targets through imperfect pairing.

One of the biggest challenges of RNA interference is the difficulty to deliver intact siRNA/miRNA across the cell membrane and into the cytosol while preserving cell viability. Intracellular delivery of RNA by transfection using peptide-based nanoparticles has shown promise. Such vectors are composed of the negatively charged nucleic acids and positively charged peptides, which co-assemble spontaneously into nanoparticles in solution. The arginine-rich peptide protamine forms nanoparticles that are predicted to exhibit good cell-penetrating properties

and lower cytotoxicity than other commercially available transfection reagents.

The naturally occurring micro-RNA miR-27a has been shown to efficiently suppress expression of the adipogenic marker PPAR (Peroxisome proliferator-activated receptor gamma), thereby blocking adipocyte differentiation [4]. For this reason, miR-27a-protamine nanoparticles may represent a new therapeutic approach to prevent metabolic complications associated with diabetes and obesity.

Since nanoparticle properties such as size and zeta potential may influence particle uptake by target cells and/or tissues *in vivo*, light scattering technologies represent an important tool to investigate the physicochemical properties of miRNA-delivery systems.

Here we demonstrate that the Litesizer™ 500 returns rapid and precise results despite very low sample concentration and volume. We used dynamic light scattering (DLS) for particle size measurement and a novel patented electrophoretic light scattering technology called cmPALS for zeta potential determination.

Mrs. ***Laura Graziano*** *graduated in 2008 in Pharmaceutical Chemistry and Technology at Università degli Studi di Milano, with specialization in Molecular Pharmacology. Afterwards she had a second level master degree in Clinical and Preclinical Drug Development at Università degli Studi di Milano Bicocca. She is working in the field of laboratory instrumentation since her graduation and she has an extensive experience in analytical chemistry, biopharmaceutical and material characterization.*

CLINICAL USE OF CANNABIS: NATIONAL AND REGIONAL REGULATORY ISSUES

Umberto Gallo

Azienda Ulss 6

At the moment, the only one cannabis-based drug registered in Italy is Sativex® spray (which is essentially an alcoholic extract, contains THC and CBD in equivalent amounts). The medicine is reimbursed by the Italian authorities, in compliance with the laws issued by the Italian Pharmaceutical Agency, exclusively for use in the treatment of moderate to severe spasticity in Multiple Sclerosis (MS) patients.

As regards cannabis-based plant products intended for medicinal use, their therapeutical relevance has been recognized in Italy since 2006, when laws that regulate the legal importation of cannabis from The Netherlands were approved. Over the years, the availability of new raw materials as well as the publication of many national and local regulations have actively contributed to increase the medical use of Cannabis, which is anyhow restricted to the "off-label" use and therefore subjected to the Law 94/98.

The Legislative Decree of 9th November 2015 from the Ministry of Health regulated the legal cultivation of medical marijuana within Italy and the dispension of galenic preparations, but the single regions were assigned to regulate the aspects related to the reimbursement.

Examining the different regional laws, a clear heterogeneity in the access to cannabis-based treatment comes to light. In particular, only 12 regions approved some regulations on the topic, nevertheless in most cases there was no practical outcome. Currently there are significant differences among regions regarding the reimbursement regimens and the methods of dispencing.

Dr. ***Umberto Gallo*** *completed his university studies at the University of Padua, graduating with laudem in Pharmacy in 1995 and qualifying, again with laudem, in Hospital Pharmacy in 1998. In the same University, in 2013 he received the title of Ph.D. after following a 3-years Course in Pharmacology, Drug therapy and Toxicology, after focusing his research study in diseases and drug interactions in old people. Among many professional roles, currently he works with responsibility in the direction of the "Servizio Farmaceutico Territoriale" of the AziendaU.L.S.S. N. 16 of Padua.*

PhD STUDENTS ORAL PRESENTATIONS

ON THE CHARACTERIZATION OF SEBS PRESSURE SENSITIVE ADHESIVES FOR THE DESIGN OF CUTANEOUS PATCHES

Gaia M.G. Quaroni

Department of Pharmaceutical Sciences, Università degli Studi di Milano, Via G. Colombo 71, 20133 Milano, Italy

Purpose: The aim of this work was to evaluate, in the design of cutaneous patches containing ibuprofen (IB), the influence of styrene-block-(ethylene-co-butylene)-block-styrene (SEBS) molecular weight (Mw) and type of tackifier, added to obtain a pressure sensitive adhesive (PSA), on: i) rheological behaviour, ii) debonding mechanisms, iii) adhesive properties and iiii) in vitro drug release rate.

Methods: Formulations differ for SEBS Mw (i.e. SOL TH®2311 - Mw = 45.61 kDa, SOL TH®2312 - Mw = 64.23 kDa and SOL TH®2315 - Mw = 176.35 kDa) and for the type of tackifier (i.e Regalite R1100® - C9 aliphatic resin and Eastotak H100W® - C5 aliphatic). For the preparation of the drug-loaded patches, IB was added at 10% (w/w). The rheological properties were obtained using a rotational rheometer, applying a frequency-sweep deformation. The debonding mechanisms on a stainless steel probe were determined by using a custom-designed probe tack tester. Patches were prepared by casting and their adhesive properties were evaluated in terms of shear adhesion and peel adhesion. The in vitro drug release rate was also determined using an adapted disk assembly method.

Results: PSAs made with low Mw SEBS behaved as viscoelastic fluids over the whole range of frequencies. The viscoelasticity is required to achieve a balance between peel and creep, crucial properties in the development of a patch. As a viscous liquid it should be able to dissipate energy during the peel process; while as a solid it should have a good resistance to shear. The failure mechanisms during the debonding process revealed that the behavior of all the PSAs was related to the relaxation time. At the lower debonding velocity they showed a liquid-like behavior with many digitations. This mechanism is required to achieve an adhesive failure without residues after the debonding process. Aiming to rationalize the selection of suitable formulations for the development of cutaneous patches, the cohesive (shear adhesion) and adhesive (peel adhesion) properties were evaluated. The shear adhesion revealed that the polymer Mw influenced the cohesive strength: increasing

SEBS-Mw, the shear adhesion values decreased. Moreover, IB caused a further reduction of the shear adhesion. However, all the patches showed an ideal cohesive strength and optimal peel adhesion, if compared to those available on market, suggesting that they will not ooze during application and could be detached without skin damage and pain upon removal. Finally, taken into consideration the biopharmaceutical performances, the percentage of IB released from the prepared patches was not influenced by SEBS-Mw and the profiles were superimposable. The drug release was completed within 24 hours according to the Higuchi pattern.

Conclusions: The overall data demonstrated the feasibility to design cutaneous patches made of SEBS. The resin type used in the preparation of SEBS-based PSA did not influence the matrix behavior. Low Mw SEBS polymer worthy of consideration because of its favorable viscoelastic behavior.

SILK FIBROIN NANOPARTICLES DRAMATICALLY REDUCE CELECOXIB IN VITRO CITOTOXICITY

Barbara Crivelli, Sara Perteghella, Laura Catenacci, Milena Sorrenti, Theodora Chlapanidas and Maria Luisa Torre

Department of Drug Sciences, University of Pavia, Viale Taramelli 12, 27100 Pavia, Italy

Purpose: Therapies based on Celecoxib (CXB) show severe toxicity events concerning cardiovascular, thrombosis and stroke risks (Dogné J.M. 2006). Encapsulation in nanosystems represents an efficient strategy to reduce toxicity phenomena related to free drug administration (Roy K. 2015; Nogueira E. 2016). This study aims to choose the best technique to obtain silk nanoparticles (SNPs) and to demonstrate the less toxicity of nano-encapsulated CXB, in an in vitro model.

Methods: Salting out or desolvation (by ethanol or acetone) methods were used to obtain SNPs loading CXB. Briefly, the first technique provides the creation of a salting solution which is mixed with the silk fibroin (SF) aqueous solution (volume ratio 1:5). As for the desolvation technique, SF solution is added drop wise into an ethanol (ratio 1:5) or acetone (ratio 1:4) bath, under magnetic stirring. All the obtained SNP suspensions were centrifuged or dialyzed to remove salts or organic solvent residues; then, SNP aqueous suspensions were freeze-dried. Multiparticulate systems were characterized in terms of particle size, morphology (SEM), drug loading, in vitro drug release and solid-state (DSC, FTIR). The nanoparticle toxicity was evaluated on both red blood cells (hemolytic assay) and human adipose derived stem cells (ADSCs): cells were incubated for 24, 48 and 72 hours with five concentrations of nanoparticles (25-200 μg/ml) or with the equivalent free drug concentration; viability was evaluated by MTT test.

Results: SNPs produced via salting out showed a mean particle size of 5 μm, meanwhile, via ethanol desolvation method, we obtained particles with a mean size distribution of 50 μm. Exploiting acetone as desolvating agent, SNPs with a diameter of about 100 nm were obtained. SEM analyses confirmed the spherical shape and size of nanoparticles. Therefore, acetone desolvation method was selected and two different drug loadings (5.5 and 11.5% w/w) were achieved. DSC and FTIR analyses indicated a high content of crystalline β-sheets, while typical absorption bands of CXB appeared in samples

characterized by higher drug content (11.5% w/w). In vitro release curves showed a starting burst culminating in a plateau after 8 hours, directly correlated to nanoparticles drug loading. The hemolytic assay showed the hemocompatibility of nanosystems, and in vitro cytotoxicity assay demonstrated the cytocompatibility of nanoparticle on ADSCs: cell viability was higher than 90 % at all the tested concentrations. Otherwise free CXB showed severe cytotoxic effects when tested at higher concentration (23-11-5.5 μg/ml, viability < 30 %).

Conclusions: Silk fibroin nanoparticles resulted effective for nanoencapsulation of celecoxib, dramatically reducing its cytotoxicity.

References

Dogné, J.M., Coxibs and cardiovascular side-effects: from light to shadow. Current pharmaceutical design 2006, 12(8):971-5.

Nogueira, E., Folate-targeted nanoparticles for rheumatoid arthritis therapy. Nanomedicine 2016, 12(4), 1113-26.

Roy, K., Molecular targets in arthritis and recent trends in nanotherapy. International Journal of nanomedicine 2015, 10, 5407-20.

NASAL REGION AS AN APPEALING ROUTE FOR BRAIN DELIVERY OF NANOENCAPSULATED STATINS

Adryana Clementino[1],[2], Sergio Souza[3] and Fabio Sonvico[1]

[1]*Food and Drug Department, University of Parma, Parma-PR, Parco Area delle Scienze 27/a, Parma - Italy*
[2]*Conselho Nacional do Desenvolvimento Cientifico e Tecnologico-CNPq, Brasilia-DF, Brazil*
[3]*Laboratório de Marcação de Células e Moléculas, Department of Radiology, Faculty of Medicine, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil*

Purpose: Statins have been strongly advocated as potentially useful class of drugs for the prevention and treatment of neurodegenerative diseases. However, past clinical trials in this direction have provided inconclusive results likely because of statins high hepatic metabolism and low permeability across the blood brain barrier, making statin delivery to the brain a challenge.1 The goal of this study was to prepare and evaluate simvastatin-loaded lecithin/chitosan nanoparticles (SVT-LCN) for nasal administration to improve brain delivery of statins by overcoming the hurdles evidenced by oral route administration.

Methods: SVT-LCN were obtained by self-assembly injecting an alcoholic solution of lecithin (2.5%) containing simvastatin (1 mg/mL) and two pharmaceutical oils into a 0.01% of chitosan aqueous solution. SVT-LCN physic-chemical properties were investigated using Dynamic Light Scattering (DLS) and Nanoparticles Tracking Analyses (NTA) for particles size and electrical superficial charge and High Performance Liquid Chromatography (HPLC) for drug loading content. In vitro drug release from raw simvastatin water suspension and nanoparticles was evaluated in a simulated nasal electrolyte solution (SNES) using dialyses bag diffusion method. Cytotoxicity of blank-LCN, SVT-LCN and raw simvastatin against human nasal RPMI2650 cells were performed using MTT-cytotoxicity assay. Biodistribution in rats after nasal administration of Tc99m-labeled SVT-LCN and simvastatin suspension was carried out via gamma scintigraphy.

Results: SVT-LCN showed particles size around 200nm, with narrow distribution (0.09±0.04), positive surface charge (+48.5±4.1) and high drug-loading capacity (98.5±1.3%). Drug release experiments were carry out for 24

hours in SNES pH 6.5 containing 0.5% of Bovine Serum Albumin to help solubilize released simvastatin and work in sink conditions. Experiments highlighted that SVT-NLC displayed a considerably faster release than the raw simvastatin suspension, with the cumulative amount released around 51.0±2.8% released by SVT-NLC formulation compare to 23.9±1.2% by the drug suspension. Blank-LCN did not present any cytotoxicity effect. Cytotoxicity of simvastatin and SVT-LCN appears to be dose-dependent. For SVT-LCN, IC50 was found to be 9.92 μM, displaying a reduced toxicity compared to the pure drug (IC50 3.50 μM). For in vivo biodistribution, a higher radioactivity fraction (>30%) was founded in the brain after the nasal delivery of SVT-LCN, in comparison to a similar administration of simvastatin suspension (< 5%) ($p<0.001$).

Conclusions: SVT-LCN presented some desirable features for nasal delivery of drugs including the optimize loading of a lipophilic drug with a good physical-chemical stability, rapid drug release and biocompatibility with the nasal mucosa. Moreover, nasal administration showed an enhanced nose-to-brain transport of SVT-LCN, opening the opportunity for brain delivery of statins for the treatment of neurodegenerative diseases.

Reference

1. Wang Q, Yan J, Chen X, et al. Statins: multiple neuroprotective mechanisms in neurodegenerative diseases. ExpNeurol 2011, 230:27–34.

SYNTHESIS AND PURIFICATION OF DESOXY-CBD PRECURSORS FOR INNOVATIVE PAIN THERAPY FORMULATIONS

*Elisa Vettorato, Giovanni Marzaro, Francesca Borgna and Nicola Realdon

Department of Pharmaceutical and Pharmacological sciences, University of Padova
**elisa.vettorato@phd.unipd.it*

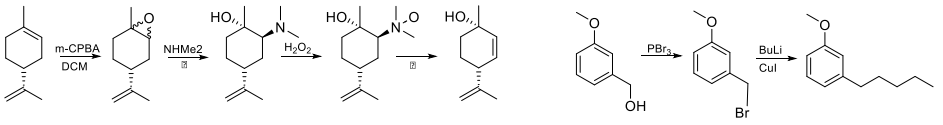
Purpose: Desoxy-CBD is a selective CB2 receptor agonist that has recently gained interest for its role in suppressing inflammation and neuropathic pain. Desoxy-CBD is also endowed with an uncommon mechanism of action since it targets the spinal glycine receptors1.

Unfortunately, this molecule is not commercially available. Hence, new synthetic and purification pathways are needed.

Methods: Based on Wilkinson, Price and Kassiou synthesis1, the precursors have been produced with a multi-step process and purified with excellent stereo selectivity.

Trans-p-mentha-1,8-dien-2-ol has been obtained from inexpensive R-(+)-limonene. The starting product was oxidized with m-chloroperbenzoic acid. The (+)-limonene oxide has been then treated with aqueous dimethylamine in a sealed vial at 90°C overnight. The cis- and trans- products formed were separated by column chromatography eluting with CH_2Cl_2/EtOAc/MeOH/NH_3 70:10:20:1. The desired trans- product has been subsequently treated with H_2O_2 to obtain a crystalline N-oxide derivative. The product was decomposed under high vacuum with a Kugelrohr oven-like system, obtaining the desired first synthon.

The second synthon, m-pentylphenol, was obtained using 3-methoxybenzylalcohol as starting product. The alcoholic function was substituted using PBr_3 and the 3-methoxybenzylbromide was condensed with n-butyllithium in presence of CuI.2 The whole synthetic strategy is reported in Scheme below.



Results: The synthesis of the first precursor, trans-p-mentha-1,8-dien-2-ol, has been developed in order to reach the maximum selectivity without any loss of starting material. The (+)-limonene oxide obtained with the first reaction was a mixture of cis- and trans- isomers, but only the trans- is the desired product for the reaction with dimethylamine. The development of a highly efficient separation method allowed to separate and collect selectively the cis- and trans- aminoalcohols, and the trans- isomer has been used for subsequent reactions. Trans-p-mentha-1,8-dien-2-ol has been obtained with excellent purity.
The other precursor, m-pentylphenol, has been obtained with fast and highly efficient reactions starting with a non-expensive compound. The efficiency of the side chain elongation reaction has been significantly raised by cooling the mixture under -5°C and keeping ah anhydrous ambient.
Conclusions: Both trans-p-mentha-1,8-dien-2-ol and m-pentylphenol, the two main precursors for desoxy-CBD synthesis, have been obtained. The first one has been isolated as a single diastereomer, but even though it showed relevant instability during each step. Further studies will be pursued to speed up the precursors synthesis and increase the whole desoxy-CBD production for innovative formulations.

References

Wilkinson, S., et al., Improved Accessibility to the desoxy analogues of Δ9-THC and CBD. Tetrahedron Lett. 2012, 54, 52-54
Petrzilka, T., et al., Synthese von Haschisch-Inhaltsstoffen. Helv. Chim. Acta 1969, 52 (4), 1102-1134.

POSTER SESSION

1. Baratta F, De Pellegrini I, Iozzino MB and Brusa P, FORMULATION, STABILITY STUDY AND QUALITY CONTROL OF A GALENIC PREPARATION FOR THE TREATMENT OF SICKLE CELL DISEASE: THE *A.P.P.A.*® PROJECT AT SAINT DAMIEN PEDIATRIC HOSPITAL IN HAITI

2. Bari E, Perteghella S, Chlapanidas T and Torre ML, PHARMACEUTICAL DEVELOPMENT OF FREEZE-DRIED EXTRACELLULAR VESICLES

3. Bellato F, Montopoli M, Vianello C, Catanzaro D, Brazzale C, Balasso A, Brunato S, Caliceti P, Salmaso S, LIPOSOMAL ACTIVE DELIVERY OF METFORMIN: A NEW TOOL IN CANCER THERAPY?

4. Bergonzi C, Saccani M, Parisi L, Galli C, Bianchera A, Bettini R, Elviri L, STUDYING CHITOSAN FILMS ENRICHMENT WITH FIBRONECTIN-APTAMERS COMPLEXES BY MASS SPECTROMETRY

5. Bertoni S, Albertini B, Dolci LS, Passerini N, A NEW STRATEGY TO IMPROVE THE ORAL BIOAVAILABILITY OF POORLY WATER-SOLUBLE APIS: DESIGN OF SELF-EMULSIFIED SPRAY CONGEALED MICROPARTICLES

6. Brunato S , Brazzale C, Mastrotto F, Alexander C, Mantovani G, Caliceti P, Salmaso S, SELF-ASSEMBLING AMINOACID-BASED COPOLYMERS FOR DOXORUBICIN CONTROLLED RELEASE

7. De Santi M, Baggio R, Realdon N, Santomaso AC, Franceschinis E, RHEOLOGICAL CHARACTERIZATION AS A TOOL TO PREDICT GRANULATION PROCESS

8. Dolci LS, Albertini B, Bertoni S, Panzavolta S, Passerini N, NOVEL MULTI-COMPOSITE SYSTEM FOR THE DELIVERY OF SODIUM ALENDRONATE TO BONE TISSUE

9. Faccendini A, Vigani B, Rossi S, Malacrida S, Bonferoni MC, Sandri G, Caramella C, Ferrari F, *IN SITU* GEL FORMING VEHICLE FOR THE DELIVERY OF *LACTOBACILLUS GASSERI* INTO VAGINAL CAVITY

10. Friuli V, Maggi L, Bruni G, Tammaro L, Conte U, POLYMER FIBERS PREPARED BY ELECTROSPINNING TO INCREASE THE DISSOLUTION RATE OF AN INSOLUBLE DRUG

11. Giordani B, Abruzzo A, Parolin C, Foschi C, Marangoni A, Fontana E, Melgoza Contreras LM, Bigucci F, Cerchiara T, Vitali B, Luppi B, *BIFIDOBACTERIUM BREVE* BC104: ORALLY ADMINISTERED VAGINAL PROBIOTIC FOR PREVENTING GENITAL AND URINARY TRACT INFECTIONS

12. Giordano LF, Manniello MD, Aquino RP, Russo P, AERODYNAMIC PROPERTIES AND DRUG SOLUBILITY OF CO-SPRAY-DRIED CLARITHROMYCIN AND N-ACETYLCYSTEINE POWDERS FOR CYSTIC FIBROSIS PATIENTS

13. Gurian E, Bonifacio A, Sergo V, SERS SPECTRA OF BIOFLUIDS: HOW PROTEIN CORONA AFFECTS THE DETECTION OF SMALL BIOMOLECULES

14. Invernizzi A, Bonferoni MC, Riva F, Sandri G, Rossi S, Caramella C, Ferrari F, TOCOPHEROL NANOEMULSION: EVALUATION ON KERATINOCYTES AND STABILIZATION AS POWDER

15. Logrippo S, Qi S, Bonacucina G, Cespi M, Pavoni L, Perinelli DR, Palmieri GF, DISEGN AND DEVELOPMENT OF AN ORODISPERSIBLE FILM AS A NEW DRUG DELIVERY FILM-SYSTEM TO DYSPHAGIC PATIENTS

16. Miele D, Bonferoni MC, Sandri G, Rossi S, Caramella C, Ferrari F, RESVERATROL LOADING IN DIFFERENT NANOPARTICLE SYSTEMS COATED WITH CHITOSAN OLEATE

17. Miele D, Sandri G, Rossi S, Bonferoni MC, Bassi B, Taglietti A, Grisoli P, Bruni G, Caramella C, Ferrari F, SILVER NANOPARTICLES LOADED ELECTROSPUN NANOFIBERS FOR WOUND HEALING

18. Musazzi UM, Poma C, POLYMERIC MICELLES FOR CUTANEOUS DELIVERY OF RESVERATROL

19. Perinelli DR, Logrippo S, Pavoni L, Pucciarelli S, Cespi M, Bonacucina G, Palmieri GF, PLGA-BASED MICROPARTICLES AS A NEW SYSTEM FOR THE TOXICOLOGICAL STUDIES OF PHTHALATES

20. Pisani S, Genta I, Dorati R, Bruni G, Conti B, DESIGN AND CHARACTERIZATION OF DEXAMETHASONE LOADED ELECTROSPUN MATRIX

21. Rossi I, Balducci AG, Colombo P, Buttini F, AOS: THE NEW ACCESSORY FOR DPI ABLE TO IMPROVE POWDER DISPERSION

22. Saporito F, Sandri G, Bonferoni MC, Rossi S, Boselli C, Caramella C, Ferrari F, HEMOSTATIC DRESSINGS LOADED TRANEXAMIC ACID IN THE TREATMENT OF BLEEDING

23. Sguizzato M, Scanelli C, de Alcantara S. de Toledo L, Luciano Bruschi M, Spizzo F, Del Bianco L, Esposito E, Cortesi R, PRODUCTION AND CHARACTERIZATION OF MAGNETIC LIPID NANOPARTICLES: A PRELIMINARY STUDY

24. Tiozzo Fasiolo L, Manniello MD, Giordano LF, Russo P and Colombo G, NANO AND MINI SPRAY-DRIED MICROPARTICLE POWDER AGGLOMERATES FOR NOSE-TO-BRAIN DELIVERY OF FLURBIPROFEN

25. Vigani B, Faccendini A, Rossi S, Bruni G, Sandri G, Bonferoni MC, Caramella C, Ferrari F, BIODEGRADABLE ELECTROSPUN ALGINATE-BASED NANOFIBERS FOR THE TREATMENT OF SPINAL CORD INJURIES

EARLY ANNOUNCEMENT

We are glad to announce that the

12TH A.It.U.N. Meeting will take place in **Bologna** in Spring 2018

Alma Mater Studiorum - University of Bologna

For up-to-date information visit: www.aitun.it

WWW.AITUN.IT