APV FOCUS GROUP DRUG DELIVERY

COMBINING SCIENCE & TECHNOLOGY TO CREATE ADVANCED DRUG DELIVERY SYSTEMS

INTERNATIONAL ASSOCIATION FOR PHARMACEUTICAL TECHNOLOGY

NEWSLETTER ISSUE 1/2015

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DRUG DELIVERY EVENTS

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◇ **1st European Conference on Pharmaceutics: Drug Delivery**
April 13-14, 2015, Reims, FR — Details

Modern Vaccines Adjuvants & Delivery Systems
May 18-20, 2015, Leiden University Medical Center, Leiden, NL — Details

The 42st Annual Meeting & Exposition of the Controlled Release Society
July 26-29, 2015, Edinburgh, Scotland, UK — Details

Suggest a meeting to be announced!

DRUG DELIVERY PRODUCTS

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Provided by Dr. Louise Rosenmayr-Templeton

HYSINGLA® ER TABLETS

In November the FDA approved Hysingla® Extended Release Tablets containing hydrocodone as the bitartrate salt [1-3]. The product from Purdue Pharmaceuticals is approved for the chronic treatment of pain that is severe enough to warrant round-the-clock opioid therapy and for which alternative treatment options are inadequate. The product is administered once daily and is available in the following dosage strengths: 20 mg, 30 mg, 40 mg, 60 mg, 80 mg, 100 mg and 120 mg. Like all opioid products the dose administered to patients must be carefully titrated to provide pain relief while minimizing side effects. Doses of 80 mg and above are not suitable for opioid-naïve patients.

The product is formulated in Purdue's proprietary extended-release solid oral platform, RESISTEC which confers abuse-deterrent properties on the tablets [3]. The technology is covered by a number of patents including one (US Patent US8,309,060) which lists Johannes Bartholomäus, a founding member of the APV Drug Delivery Focus Group, as one of the inventors. The tablets are difficult to crush, break or dissolve and the components form a viscous hydrogel that is too thick to pass through a hypodermic needle if attempts are made to prepare an injectable form. The product also has the advantage that it contains only hydrocodone as the therapeutic entity and does not also contain paracetamol which limited the dose of earlier hydrocodone products.

A double-blind placebo controlled clinical study of Hysingla® Extended Release Tablets demonstrated the efficacy and safety of the product [1]. In total 905 patients (opioid-naïve and opioid-experienced) with chronic low back pain were enrolled in the 45-day open-label conversion and dose titration phase. Of these 588 proceeded to the double-blind phase (50% in the active arm and 50% in the placebo). The product provided statistically significant greater analgesia than placebo. Purdue also carried out a number of abuse deterrence studies in line with the requirements of the FDA's

draft guidance on Abuse-Deterrent Opioids — Evaluation and Labeling [4] that showed that the abuse-deterrent features of Hysingla ER reduced the potential for certain types of abuse (oral, snorting and injection).
Purdue has launched Hysingla ER in the US in January 2015; Press Release from Jan 26, 2015: http://www.purduepharma.com/news-media/2015/01/hysingla-er-hydrocodone-bitartrate-extended-release-tablets-cii-now-available/

MYSIMBA® PROLONGED RELEASE TABLETS

Mysimba prolonged release tablets from Orexigen Therapeutics containing 8 mg naltrexone and 90 mg bupropion received a positive review from the EMA's Committee for Medicinal Products for Human Use (CHMP) in Dec 2014 [5]. The tablets are indicated as an adjunct to a reduced-calorie diet and increased physical activity for the management of weight in adult patients with a BMI of ≥ 30 kg/m² (obese), or ≥ 27 kg/m² to < 30 kg/m² (overweight) in the presence of one or more weight-related comorbidities (e.g., type 2 diabetes, dyslipidaemia, or controlled hypertension). The standard dose is two tablets twice daily but patients new to the medication are started on one tablet per day and the dose is gradually increased over a period of 4 weeks. The tablets have a trilayer core composed of two drug layers, containing the drug and excipients. These are separated by a more rapidly dissolving inert layer.

Naltrexone is a mu-opioid antagonist and bupropion is a norepinephrine and dopamine reuptake inhibitor. Both compounds affect eating behaviour centrally through their action on parts of the brain involved in the control of food intake and energy expenditure, and for the reward pathways associated with eating food. In four pivotal clinical studies in which patients, in addition to diet and exercise counseling, were treated with Mysimba for around 12 months, the product was shown to result in weight lost that was clinically relevant. The product should be administered with food but not a high fat meal as this increases significantly the absorption of the actives [6].

The product is already marketed in the US as Contrave® by Takeda, which licensed the product form Orexigen.

References and Further Information

[1] Entry for Hysingla® ER Tablets on Drugs@FDA. http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Label_ApprovalHistory#labelinfo (Accessed on 23.02.2015).

[2] FDA approves extended-release, single-entity hydrocodone product with abuse-deterrent properties (Accessed on 23.02.2015).

[3] Purdue Pharma L.P. Receives FDA Approval for Hysingla™ ER (hydrocodone bitartrate) Extended-Release Tablets CII, A Once-Daily Opioid Analgesic Formulated with Abuse-Deterrent Properties. http://www.purduepharma.com/news-media/2014/11/purdue-pharma-l-p-receives-fda-approval-for-hysinglatm-er-hydrocodone-bitartrate-extended-release-tablets-cii-a-once-daily-opioid-analgesic-formulated-with-abuse-deterrent-properties/ (Accessed on 23.02.2015)

[4] Abuse-Deterrent Opioids — Evaluation and Labeling. http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm334807.htm. (Accessed on 23.02.2015)

[5] Committee for Medicinal Products for Human Use's Summary of Opinion for Mysimba. http://www.ema.europa.eu/docs/en_GB/document_library/Summary_of_opinion_-_Initial_authorisation/human/003687/WC500179589.pdf (Accessed on 23.02.2015)

[6] Entry for Contrave on Drug@FDA http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails (Accessed on 23.02.2015)

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Provided by Kaspar van den Dries, PhD, Patheon, Contact: Kaspar.vdDries@Patheon.com

XSPRAY MICROPARTICLES AB (Solna, Sweden)

XSpray is specialized in the formulation of protein kinase inhibitors (PKI's), many of which suffer from formulation-related medical problems. XSpray's HyNap™ is a PLATFORM TECHNOLOGY that addresses the formulation-related drawbacks of small molecule PKI's and can improve the solubility and bioavailability of even the most challenging drug substances.

The company was founded in 2003 (originally as CENS Delivery AB), and focused on developing a new technology enabling the production of nano-scale particles for use in drug production. In February 2007 the company name was changed to XSpray to reflect the change in focus from research to commercialization of the technology for use in the production of high quality pharmaceutical particles. After achieving successful lab and scalability results, a decision was made in late 2007 to develop a GMP production facility. In 2008, solid state characterization and analysis services were added to the company's offering. In 2009, XSpray doubled the size of its service lab and increased its personnel

resources to meet growing interest in the company's offering. XSpray's GMP production facility was opened in mid-2009, providing customers with high quality drug particles and powders for use in their clinical studies.
Next to the focus on formulation of PKI's, XSpray makes its proprietary technologies available in a variety of ways - contract services, evaluation/joint development projects, characterization services and GMP production, as well as offering additional partnering and licensing opportunities.

Fact sheet:

Founded:	2003
Location:	Solna, Sweden
Ownership:	Majority ownership of XSpray is held by Karolinska Development AB.
Employees:	Unknown
Key technology:	XSpray RightSize™, a spray drying technology based on supercritical fluid as anti-solvent. A patented two liquid nozzle systems where rapid mixing of cosolvent- super critical antisolvent leads to the formation of very fine particles. The size and polymorph of the produced particles is controlled by simply varying process parameters, such as the solvent used, temperature and pressure
Products:	Nilotinib and other protein kinase inhibitors described for the treatment of cancer.
Development status:	Phase I trial utilizing HyNAP™ of nilotinib has been completed comparing pharmacokinetics of current formulation in the fed and fasted state.
Partnerships:	Unknown
Website:	http://www.xspray.com
Contact:	XSpray Microparticles AB Gunnar Asplunds allé 32 SE-171 63 Solna Sweden Phone: +46 (0)8 730 37 00 e-mail: info@xspray.com

DRUG DELIVERY PEOPLE

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Provided by Prof. Dr. Karsten Mäder

DARRAGH MURNANE has a degree in Pharmacy from Trinity College Dublin (Ireland) and obtained a PhD in Pharmaceutics at King's College London (UK) under the supervision of Profs. Gary Martin and Chris Marriot. In 2007 he was appointed as a Lecturer in Pharmaceutics at King's College London (UK) and then joined the University of Hertfordshire (UK) in 2010 as a Principal Lecturer in Airways Pharmaceutics.

Darragh's research area is focussed on drug delivery to the airways including the lung, nose and the mouth-throat cavities. His work combines chemical engineering, physical and analytical chemistry approaches to understand the link between patient physiology and drug targeting to the airways. This extends to developing formulation analysis tools to aid identification of medicines and formulation performance. This has extended to investigations into patient use of inhaled therapies and has led to a number of collaborations with clinicians and pharmaceutical companies.

Since 2013, Darragh has held the position of President of the Aerosol Society and represents the UK and Ireland at the European Aerosol Assembly. He is also a member of the inhalation focus group of the Academy of Pharmaceutical Sciences and the scientific review panel for the annual Drug Delivery to the Lungs conference, Europe's largest annual inhalation conference.

Darragh is currently organizing a joint Academy of Pharmaceutical Sciences-Aerosol Society Symposium on strategies to demonstrate bioequivalence in inhaled medicines development bringing together Europe's leading regulators and industrial and academic researchers (http://www.apsgb.co.uk/EVENTS/20150330/).

Drug Delivery Systems Used To Deliver Opioids in Chronic Pain Therapy
Part IV: Transmucosal systems

By Johannes Bartholomäus, Burghöhenweg 5, 52080 Aachen

5. Transmucosal formulations to treat breakthrough pain

Technical solutions by drug delivery systems

This article is the fourth in a series dealing with drug delivery systems used to deliver opioids in chronic pain therapy. The first of these articles appeared in Issue 1/2011 of this Newsletter and covered oral prolonged release systems; the second in Issue 3/2012 dealt with transdermal systems; the third in Issue 2/2013 focused on parenteral depot systems and devices. The aim of the articles was to demonstrate how drug delivery systems have been employed to extend the dosing interval of chronic pain treatment from several times per day to once or twice per week and, in the case of implanted pumps even up to some months, by keeping blood concentrations more or less constant over time. A change in the basic chronic pain level can then be treated by increasing or sometimes also decreasing the opioid dose in the delivery systems. However, pain is not always constant – not even over the course of one day – and breakthrough pain episodes often occur. Sometimes such peak pains can be expected e.g. if a bedridden patient has to be turned but mostly they occur without warning (Table 1).

Table 1: Predictability of breakthrough pain episode

Predictable	Percentage of cases
always	15 %
nearly always	11 %
often	7 %
sometimes	19%
never	48 %

(Source: Portenoy et al., Pain 81 (1-2): 129-134, 1999)

Breakthrough pain seems to occur in cancer patients more often than in non-malignant terminal disease patients. Zeppetella et al. found for cancer patients that 89% of patients who suffered from chronic pain also experienced breakthrough pain episodes [J Pain Symptom Manage. 2000 Aug;20(2):87-92]; whereas in non-malignant terminal disease, 63% of pain suffering patients recognized breakthrough pain [Palliat Med. 2001 May;15(3):243-6]. For cancer pain patients the number of breakthrough pain episodes per day as well as their duration is illustrated in Figs. 1 and 2 respectively. More than 50% of such patients faced 2 – 4 attacks per day which could be of different duration. About 50% of the attacks persisted longer than 20 min but only about 6% lasted longer than 90 min.

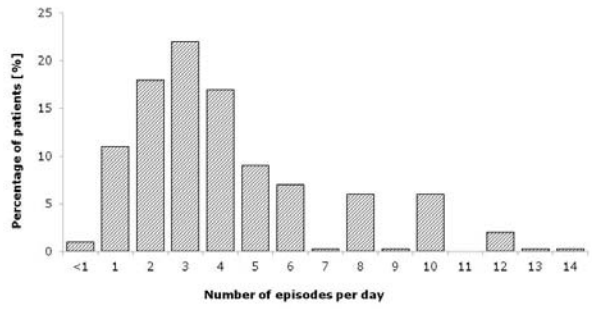

Figure 1: Frequency of breakthrough pains
(Source: After Zepettella et al, 2000)

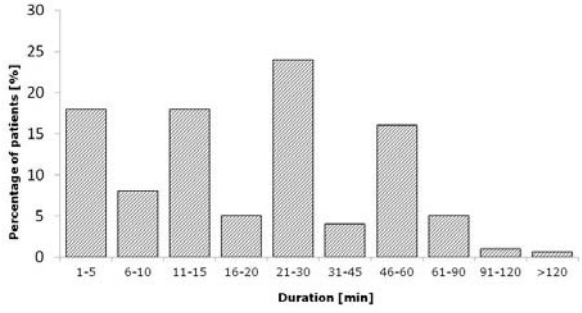

Figure 2: Duration of breakthrough pains
(Source: After Zepettella et al, 2000)

In order to treat breakthrough pain the opioid should be rapidly available at the site of action. Intrathecal bolus injections at the request of the patient are the fastest possible method of opioid delivery but only work for patients with implanted drug pumps (see part III of this series). Of course an iv injection would lead to nearly instant availability in the bloodstream and fast onset of action after passage through the blood brain barrier. However, most people do not like frequent injections and in most cases the nursing staff who could administer an iv injection are not readily available. Thus, iv injection is not the ideal administration pathway to cure such pain. On the other hand, peroral administration would not be meet the requirement of rapid pain relief because of the long gastro-intestinal transit time prior to the drug reaching the site of absorption. However, transmucosal administration via sublingual, buccal or pulmonary tissue could be fast enough depending on the transmucosal permeability and dose of the opioid. So low dose opioids like buprenorphine or fentanyl seem to be suitable candidates. From these candidates fentanyl exhibits a faster transmucosal absorption leading to a Tmax of about 20 – 30 min following sublingual or buccal absorption compared with a Tmax for buprenorphine is about more than 60 min. Thus, a variety of fentanyl transmucosal drug delivery systems have been

introduced for breakthrough pain treatment. These include sublingual tablets, lozenges on a stick, buccal effervescent tablets and films and nasal sprays. As breakthrough pain is very individual and the right dose for the patient needs to be found (often by titration) a wide range of fentanyl doses is available with 100 µg (only for sublingual tablets), 200 µg, 300 µg (only for sublingual tablets), 400 µg, 600 µg, 800 µg, 1200 µg (only for lozenges and films) and 1600 µg (lozenges only) for the formulations used in the oral cavity and 50 µg, 100 µg and 200 µg for nasal administration. While perorally swallowed fentanyl shows a bioavailability of about 30%, transmucosal administration raises bioavailability to 50 – 90% depending of the type of formulation and administration (Table 2).

Table 2: Bioavailability of different fentanyl transmucosal formulations

Formulation	**Bioavailability**
Peroral tablet (swallowed)	31 %[1]
Lozenge on a stick (buccal)	47 %[1]
Effervescent tablet (buccal)	65 %[1]
Film/strip (buccal)	71 %[2]
Nasal spray	89 %[3]

(Sources: [1] Darwish et al., J Clin Pharmacol. 2007 Mar;47(3):343-50, [2] Fachinformation Breakyl®, [3] Fachinformation Instanyl®)

Sublingual fentanyl tablets (e.g. Abstral®) are made by simple compression of blend/granules of mannitol, silicified MCC, croscarmellose-Na and Mg stearate as excipients and are intended to dissolve under the tongue. Actiq® lozenges on a stick are intended to be put into the buccal cavity and sucked. They are made by compression of a blend/granules of hydrolyzed starch, citric acid, disodium hydrogen phosphate, berry flavor and Mg stearate. The lozenge is glued to the stick by use of an aqueous mixture of poly-(O-[hydrogen-(oct-1-en-1-yl)succinyl] starch sodium, sucrose and corn starch. It is recommended to move the lozenge in the buccal cavity close to the cheek by means of the applicator to maximize the contact area. The lozenge should be sucked and not chewed to assure the higher bioavailability (here 47%) by transmucosal absorption compared to swallowed fentanyl. If at the end of application material remains on the stick this should be flushed with warm water from the stick into a sink to avoid any misuse afterwards. By the way, although this formulation because of its mode of administration was sometimes called lollypops, it does not look like an attractive candy and this was intended to prevent from accidental use by children (Fig. 3).

Figure 3: Actiq Lozenge on a stick (Source: own photograph)

In 2006 (USA) and 2008 (EU) Effentora® (EU, in USA: Fentora®) was approved. This formulation was a slightly effervescent buccal tablet (excipients: mannitol, carboxymethyl starch-Na, sodium (bi)carbonate, citric acid, Mg stearate) with faster absorption (Fig. 4) and higher bioavailability (Tab. 2). These features were assigned to the effervescent design with citric acid and carbonic acid as a reaction product lowering the pH inside the tablet and, thus, increasing solubility and dissolution speed of fentanyl in its ionized form while in a second step outside the tablet at saliva pH, the carbonic acid disintegrates into carbon dioxide and water and fentanyl changes more to the non-ionized form enabling faster transmucosal permeation. The onset of efficacy could be detected by about 10 minutes reaching maximum pain relief after 45 – 60 minutes (Source: Slatkin NE *et al*. J Support Oncol 2007;5:327-334).

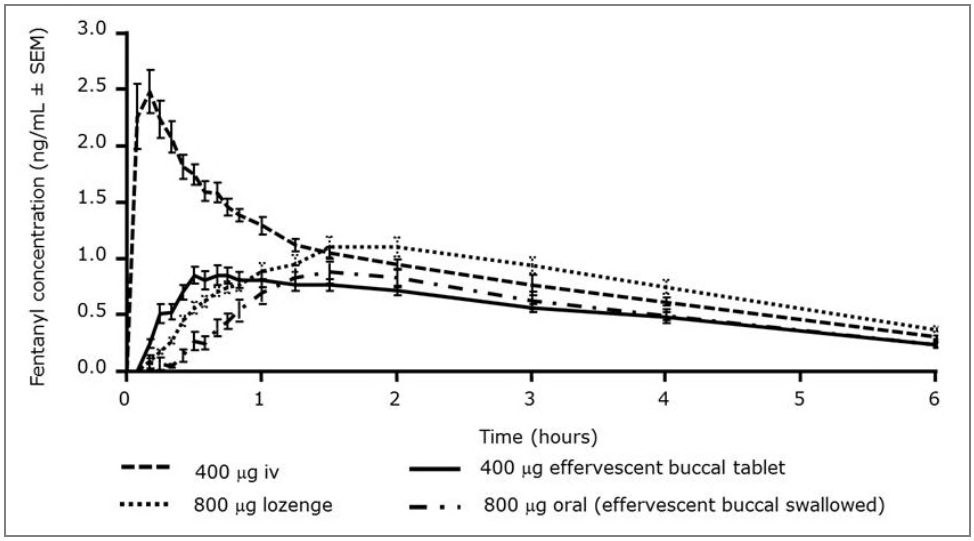

Figure 4: Serum concentration of fentanyl after administration of different dosage forms (Source: After Darwish M *et al.* J Clin Pharmacol 2007;47:343-350)

In 2013 with Breakyl® (EU, in USA: Onsolis®, discontinued) a buccal film formulation of fentanyl (described also in APV Drug Delivery Newsletter Issue 1/2014) was introduced. This formulation was the first buccal two layer film with one layer containing the active intended for direct contact to buccal mucosa and a second slower dissolving layer as a backing shielding the system from the remaining oral cavity and forcing unidirectional release to the buccal mucosa.

With Instanyl® a phosphate buffered aqueous solution of fentanyl became available for nasal administration. Due to the low amounts (50 – 200 µg) and the extremely high permeability of fentanyl a fast (Tmax 12 – 15 min) and nearly complete (89% bioavailability) transmucosal absorption was achieved.

By the end of the 90ies and during the 2000s pulmonal administration of morphine and/or fentanyl was in phase I development by using either the AerX® (by Aradigm) or the Staccato® (by Alexza) drug delivery system. AerX® made use of aerosolization of drug solutions by a device mechanically ejecting the solutions from blisters through laser-drilled nozzles of a few µm integrated in the blisters and forming droplets of 1 – 6 µm size. Staccato® achieves aerosolization by sublimation via heating a stainless steel substrate coated with pure active drug for some milliseconds to about 400 – 500°C, vaporization of the active into the inhalation airstream passing through the device and instantaneous condensation of the active as small particles of low µm size in that airstream allowing deep lung administration. Although both systems showed extremely fast drug administration into the systemic blood stream virtually comparable to iv injection no pharmaceutical company took up these delivery systems for a full development and marketing authorization with an opioid.

Currently sufentanil sublingual tablets are under development for patient controlled analgesia (PCA) after surgical procedures as an alternative to iv PCA pumps (Zalviso®). For this treatment the sublingual tablets are administered via a medical device that controls the amount of tablets used in a certain time period and allows a follow-up administration only after a predefined lock-out time after the previous tablet. For PCA Zalviso® was filed for marketing authorization in USA and EU and is waiting for approval. In another development program the sublingual tablets have been successfully investigated in a Phase II study in breakthrough pain. One advantage of sufentanil compared to fentanyl might lay in the shorter plasma half-life of the compound as breakthrough pain is short-term pain that probably does not require long lasting increased opioid concentrations compared to the basic chronic pain treatment already provided by extended release tablets or transdermal patches.

From Technical Solutions to Commercial and Environmental Factors and back

Oral prolonged release formulations of opioids with up to once daily administration and transdermal patches with twice or once weekly administration are dosed to balance the needs of pain relief with the appropriate degree of side effects e.g. sedation. They often form the basis of analgesia for chronic pain supporting a better quality of life. But as pain is not always constant over the day breakthrough pain episodes may impair the quality of life of patients, especially cancer pain patients. To treat such episodes in the right manner is not an easy task as they occur often unexpectedly and range in duration from less than 5 minutes to up to 2 hours while the appearance of the analgesic compound in effective concentrations at the site of action takes at least ten minutes with a Tmax of 20 - 30 min and more when administered transmucosally. Clinical studies provided some evidence that statistically significant pain relief compared to placebo starts at about 10 minutes after administration taking about 45 – 60 minutes to reach its maximum. Hence, since each patient experiences breakthrough pain differently also the therapy has to be individualized meaning there it is critical to provide training to doctors, nurses and other carers as well as obtaining frequent feedback from the patient. Thus, selection of the right formulation and the right dose strengths is often not easy and for some patients there even may be no adequate treatment using the available products. By the way, pricing of the transmucosal products shows (at least in Germany) the peculiarity that all the different fentanyl dose strengths of a formulation type are the same price (Source: Rote Liste) as opposed to the typical situation of most drug products that the price increases with the dose strength. So costs are per individual pain episode independent of necessary dose strength. At least in Europe the market for breakthrough pain products is only a small sector of the market for opioids in chronic pain which is dominated by oral extended release products and patches. In the USA annual sales of transmucosal fentanyl has grown (e.g. >500 Mio $ for Actiq) but the products and their promoters are facing public criticism and litigations for example on off-label use. So there is still a need to find the best treatment of patients undergoing breakthrough pain.

6. Concluding Remarks

What happened over the last years?

Since the time this series of featured articles started at the beginning of 2011, there has been some changes and/or progress. E.g. in Part II on transdermal patches it was reported that the CHMP denied marketing authorization of a generic fentanyl patch that was larger in size and lower in drug utilization than the originator product. Such requirements are now set as state-of-the art for generic patches by the recently published "Guideline on quality of transdermal patches" (EMA/CHMP/QWP/608924/2014).

As another example, in Part I on oral prolonged release products it was mentioned that especially in the USA there was a demand for abuse deterrent formulations that could help deal with the abuse of prescription opioids. For example in late 2011 the new extended release opioid tapentadol was introduced to the USA in a crush-resistant formulation

(Nucynta® ER) and at the beginning of 2012 the original Opana® ER was also replaced by a crush-resistant tablet. In January 2013 the FDA has a draft "Guidance for Industry: Abuse-Deterrent Opioids —Evaluation and Labeling" setting out i.a. framework for the development of abuse-deterrent opioid formulations, categories for their in-vitro and in-vivo characterization and potential labeling of such products. As also described in Part I OxyContin® was reformulated into a matrix tablet with increased crushing resistance and the FDA wanted follow-up studies investigating the influence of the new product on the abuse environment. So e.g. an assessment utilizing data from the National Addictions Vigilance Intervention and Prevention Program (NAVIPPRO) sentinel surveillance network showed that the proportion of individuals abusing OxyContin® by any administration route declined from 24% among all prescription opioid abusers to 12% for the 11-month period after introduction of the reformulation. With respect to routes of application in abuse the percentage for the oral route declined from 14% to 10% whereas abuse via non-oral routes that require tampering (e.g. injection, intranasal, smoking) declined by 73% from 18% to 5% in individuals abusing any prescription opioid (Source: Black R et al. Effects of reformulated OxyContin® among patients assessed for substance abuse treatment in the NAVIPPRO sentinel surveillance network. J Pain. 2012;13:S58). In addition, drug liking studies e.g. by nasal administration (a typical way of abuse) comparing oxycodone powder and manipulated original and reformulated OxyContin® demonstrated less liking of the manipulation product from new formulation than for the powder or the manipulated original formulation. FDA finally assigned a label describing the results of the abuse-deterrence characterization to OxyContin® and decided not to accept or approve any generic forms of the original OxyContin® ER since the original product was removed from the market for reasons of safety or effectiveness.

When later Zohydro® a new twice daily extended release product containing hydrocodone in a conventional pellet formulation was approved by the FDA and marketed as a new opioid in chronic pain there was a public outcry that such products should not be allowed without abuse-deterrence features. Thus, the company marketing Zohydro® promised to reformulate the product in a two-step approach parallel to marketing the original product. The first step involved adding a viscosity increasing principle which became effective if the product is manipulated for e.g. iv abuse. This was approved by the FDA in Jan 2015 and the second step intended to add more abuse-deterrence features is under development. On the other hand a new once daily hydrocodone extended release product Hysingla® was approved by FDA in November 2014 and introduced by another company in an abuse-deterrent crush-resistant formulation right from the beginning.

So, abuse-deterrent features are becoming more and more standard at least for extended release formulations in the USA. However, it has to be borne in mind that absolute prevention of abuse of opioids by a drug formulation is virtually impossible since this would mean that the drug will not be released and, thus, the patient will not receive therapy. Therefore, abuse-deterrent formulations have to fulfill a double requirement: Of capital importance, the formulation must deliver the active ingredient to the patient in a safe and effective manner, allowing treatment of the patient's pain when taken in the intended way. Subordinated, the formulation must raise hurdles to distract the abuser from abuse of the formulation but without having those hurdles negatively impacting the safe and effective delivery to the eligible patient. Abuse-deterrent formulations have to be considered firstly from a patient centric perspective and secondly from society's perspective on potential abuse. They cannot solve the age old problem of addiction to opioids as opioids are also available from a lot of other (illegal) sources but they may allow safer access to patients in need of opioids for pain treatment.

Why so many different delivery systems?

Pain is a very individual experience as expressed by one of the most pragmatic definitions of pain attributed to Margo McCaffery, a pain nurse. She described pain as "whatever the experiencing person says it is, existing whenever and wherever the person say it does." This definition emphasizes that pain is highly individual and therefore also therapy has to be highly individualized. So there is no one size fits all solution for pain and the general conclusion and appeal is:

"It is the duty of all analgesic drug delivery systems and the people developing, marketing, prescribing and administering them to serve the relief of patients from their pain!"

This Part IV finalizes the series of featured articles on "Drug Delivery Systems Used to Deliver Opioids in Chronic Pain Therapy".

DRUG DELIVERY LITERATURE

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Provided by Dr. Carsten Timpe

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ABOUT THE FOCUS GROUP

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The APV Drug Delivery Focus Group (APV DD) is a section of the APV (Arbeitsgemeinschaft für Pharmazeutische Verfahrenstechnik e.V. / International Association for Pharmaceutical Technology), a major European society for those sharing a professional interest in pharmaceutical sciences. The Focus Group was established in 2003 in response to the increasing importance of drug delivery within modern pharmaceutics.

Read more. ***Contact us.***

COMBINING SCIENCE AND TECHNOLOGY TO CREATE ADVANCED DRUG DELIVERY SYSTEMS

OUR MISSION STATEMENT:

Modern drug delivery research and development is a truly multidisciplinary approach and must combine all relevant scientific, technical, medical and regulatory aspects required for the design, preparation, testing, manufacturing and registration of drug delivery systems and their components. It is the mission of the APV Drug Delivery Working Group to foster and promote all aspects of research and development required to transform drug molecules into safe, applicable and acceptable drug delivery systems, which provide therapeutic benefit, convenience to the patient and improve patient compliance.

Our mission includes in particular the following tasks:

- Thoroughly understanding the physical-chemical and biopharmaceutical properties of the drug substance to be delivered and the components of the drug delivery system
- Understanding the biological barriers and the interactions of the drug molecule and its delivery system with the biological environment and the biological target including PK/PD and PK/safety relationships
- Research on excipients, materials and technologies required for the design, preparation and manufacturing of drug delivery systems for a selected route of administration
- Development and understanding of methods for in vitro and in vivo evaluation of drug delivery systems and their components
- Knowledge of regulatory requirements for clinical testing, manufacturing and registration of drug delivery systems

All disciplines relevant to the above mentioned areas of drug delivery R&D are invited to contribute to the APV Drug Delivery Group:

Pharmaceutics, Biopharmaceutics, Analytics, Biology, Physical Chemistry, Biochemistry, Physics, Engineering Sciences, Nano Technology, Material Sciences, Polymer Science, Toxicology, Drug Safety, Clinical Research, Drug Regulatory Affairs, etc.

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