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Nachrichten und Mitteilungen

International Association for Pharmaceutical Technology
Arbeitsgemeinschaft für Pharmazeutische Verfahrenstechnik e.V.
Gemeinnütziger wissenschaftlicher Verein

APV NEWS
04 · 2022

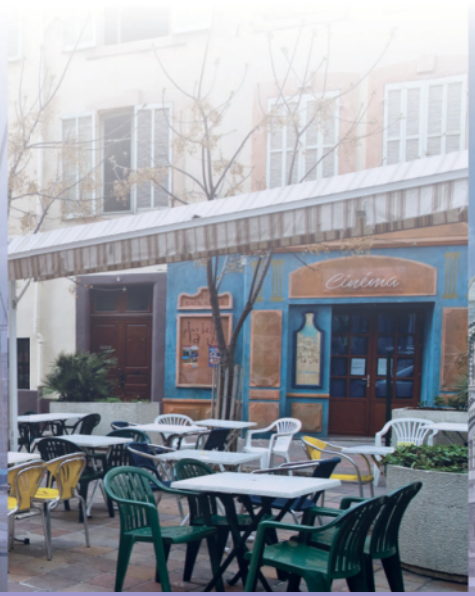
4th European Conference on Pharmaceutics

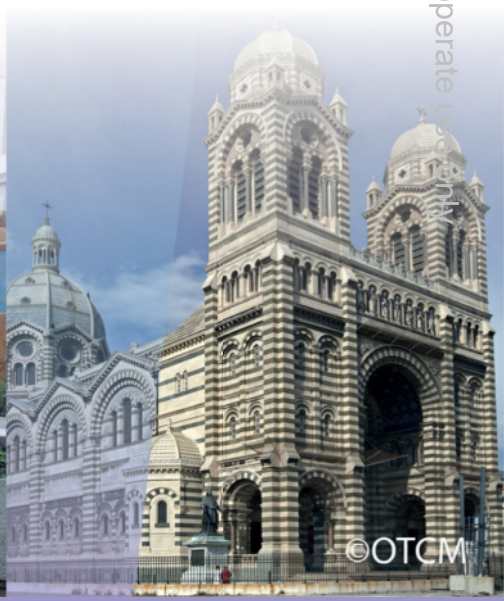
4th European Conference on Pharmaceutics

Advanced technologies enabling new therapies

Marseille France

20 - 21 March 2023





Lokale Gruppen

Mittwoch, 28. September 2022

Lokale APV-Gruppe Rhein-Main ab 19:30 Uhr. Der Veranstaltungsort wird noch bekanntgegeben. Weitere Informationen und Angaben zu dem Veranstaltungsort sowie den nächsten Terminen erhalten Sie bei Cathrin Pauly (pauly@aspiras.de).

Lokale APV-Gruppe Berlin

Weitere Informationen und Angaben zu den nächsten Terminen erhalten Sie bei Dr. Andreas Sachse (andreas.sachse@cpl-sachse.de).

Lokale APV-Gruppe Ulm/Biberach/Ravensburg/Bodensee

Weitere Informationen und Angaben zu den nächsten Terminen erhalten Sie bei Dr. Martin Müller (martin.mueller@vetter-pharma.com).

Lokale APV-Gruppe Basel

Weitere Informationen und Angaben zu den nächsten Terminen erhalten Sie bei Dr. Lars Restetzki (lars.restetzki@roche.com).

Lokale APV-Gruppe Rhein-Neckar

Weitere Informationen und Angaben zu den nächsten Terminen erhalten Sie bei Dr. Viktoria Riedel (viktoria.riedel@schwabe.de).

Lokale APV-Gruppe Westfalen

Weitere Informationen und Angaben zu den nächten Terminen erhalten Sie bei Dr. Johanna Anlahr (johanna.anlahr@bayer.com).

Lokale APV-Gruppe Nordrhein

Weitere Informationen und Angaben zu den nächten Terminen erhalten Sie bei Klaus Wening (klaus.wening@grunenthal.com).

Lokale APV-Gruppe Mecklenburg-Vorpommern

Weitere Informationen und Angaben zu den nächten Terminen erhalten Sie bei Katharina Tietz (katharina.tietz@uni-greifswald.de).

Lokale APV-Gruppe Oberbayern

Weitere Informationen und Angaben zu den nächsten Terminen erhalten Sie bei Dr. (USA) Julia Schulze-Nahrup (jsn@pharmoveo.de).

What´s hot in European Journal of Pharmaceutics and Biopharmaceutics?

Elena Richert, Ludwig-Maximilians-Universität, D-München

The role of intrinsic fines in the performance change of expired lactose carriers for DPI applications

Nicholas Bungert, Mirjam Kobler, Regina Scherließ

Dry powder inhalation offers a well-established administration route for either local or systemic drug delivery. Lactose-based powder blends still build the basis of respiratory drug delivery, despite of numerous emerging formulation approaches. The amount of fine lactose excipients, either extrinsic or intrinsic, crucially influences the aerodynamic performance of the corresponding blend. This study highlights the role of intrinsic fines as a fundamental performance affecting parameter during storage and expiry of lactose carrier bulk. We showed that intrinsic fines play an inferior role after expiring compared to fresh batches. If strongly adhering or even merged fines regain their mobility and contribute to the dispersion (by removal and re-addition), it will significantly enhance drug delivery. Furthermore, we provide evidence for decreased mobility of intrinsic fines caused by humidity (e.g., during inappropriate storage) resulting in decreased powder fluidisation.

Needle clogging of protein solutions in prefilled syringes: A two-stage process with various determinants

Stefan Scheler, Simon Knappke, Michael Schulz, Alexander Zuern

Clogging of staked-in-needle prefilled syringes (PFS) is a sporadic and scarcely predictable event, which occurs particularly in highly concentrated protein solutions and can result in the injection of incomplete doses, especially if autoinjector devices are used for administration. A systematic screening of possible causes and triggers was performed in order to find the crucial factors of influence, the underlying mechanisms and possible measures for prevention. An essential prerequisite for the formation of a solidified clog in the needle is the ingress of liquid from the barrel, which was investigated and quantified by means of neutron imaging after storage of prefilled syringes under various conditions. The needle filling ratio increases with both the storage temperature and the storage period, as a result of atmospheric gas diffusion through the needle shield. While the air pocket in the needle is reduced by this process, diffusion of water vapor does not affect the filling ratio but instead increases the protein concentration in the needle lumen, leading to an exponential rise of the viscosity and finally to the solidification of the protein solution. Maintaining the air pocket in the needle by avoiding any diffusion promoting pressure gradient is therefore the most effective protection from clogging.

Structured solubility behaviour in bioequivalent fasted simulated intestinal fluids

Qamar Abuhassan, Ibrahim Khadra, Kate Pyper, Patrick Augustijns, Joachim Brouwers, Gavin W. Halbert

Drug solubility in intestinal fluid is a key parameter controlling absorption after the administration of a solid oral dosage form. To measure solubility in vitro simulated intestinal fluids have been developed, but there are multiple recipes and the optimum is unknown. This situation creates difficulties during drug discovery and development research. A recent study characterised sampled fasted intestinal fluids using a multidimensional approach to derive nine bioequivalent fasted intestinal media that covered over 90% of the compositional variability. These media have been applied in this study to examine the equilibrium solubility of twenty one exemplar drugs (naproxen, indomethacin, phenytoin, zafirlukast, piroxicam, ibuprofen, mefenamic acid, furosemide, aprepitant, carvedilol, tadalafil, dipyridamole, posaconazole, atazanavir, fenofibrate, felodipine, griseofulvin, probucol, paracetamol, acyclovir and carbamazepine) to determine if consistent solubility behaviour was present. The bioequivalent media provide in the majority of cases structured solubility behaviour that is consistent with physicochemical properties and previous solubility studies. For the acidic drugs (pKa < 6.3) solubility is controlled by media pH, the profile is identical and consistent and the lowest and highest pH media identify the lowest and highest solubility in over 70% of cases. For weakly acidic (pKa > 8), basic and neutral drugs solubility is controlled by a combination of media pH and total amphiphile concentration (TAC), a consistent solubility behaviour is evident but with variation related to individual drug interactions within the media. The lowest and highest pH × TAC media identify the lowest and highest solubility in over 78% of cases. A subset of the latter category consisting of neutral and drugs non-ionised in the media pH range have been identified with a very narrow solubility range, indicating that the impact of the simulated intestinal media on their solubility is minimal. Two drugs probucol and atazanavir exhibit unusual behaviour. The study indicates that the use of two appropriate bioequivalent fasted intestinal media from the nine will identify in vitro the maximum and minimum solubility boundaries for drugs and due to the media derivation this is probably applicable in vivo. These media could be applied during discovery and development activities to provide a solubility range, which would assist placement of the drug within the BCS/DCS and rationalise drug and formulation decisions.

Structure-based peptide ligand design for improved epidermal growth factor receptor targeted gene delivery

Simon Decker, Alexander Taschauer, Emanuela Geppl, Viktoria Pirhofer, Michael Schauer, Stephan Pöschl, Florian Kopp, Lars Richter, Gerhard F.Ecker, Haider Sami, Manfred Ogris

The epidermal growth factor receptor EGFR allows targeted delivery of macromolecular drugs to tumors. Its ligand, epidermal growth factor, binds EGFR with high affinity but acts mitogenic. Non-mitogenic peptides are utilized as targeting ligands, like the dodecapeptide GE11, although its low binding affinity warrants improvement.

We applied a two-step computational approach with database search and molecular docking to design GE11 variants with improved binding. Synthesized peptides underwent binding studies on immobilized EGFR using surface plasmon resonance. Conjugates of peptides coupled via heterobifunctional PEG linker to linear polyethylenimine (LPEI) were used for transfection studies on EGFR-overexpressing cells using reporter gene encoding plasmid DNA.

Docking studies unraveled similarities between GE11 and the EGFR dimerization arm. By skipping non-overlapping amino acids, a less hydrophobic segment (YTPQNVI) was identified to be directly involved in EGFR binding. By replacing valine by tyrosine, a full-length version with proposed enhanced binding (GE11m3) was developed. While hydrophobic or hydrophilic segments and variations thereof exhibited low binding, GE11m3 exhibited 3-fold increase in binding compared to GE11, validating in silico predictions. In transfection studies, polyplexes with GE11m3 induced a significantly higher reporter gene expression when compared to GE11 polyplexes both on murine and human cancer cells overexpressing EGFR.

Impressum:

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Anna-Maria Pötzl · APV e.V.

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Hersteller/Typ	Listenpreis	mtl. Rate
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CUPRA Born 150kW204PS 58kWh Automatik inkl. Pilot M+ Pack, BeatsAudioTM Soundsystem, Cargo Pack, Heat pump, Skyline Roof, Tech L Pack, Privacy Glass, Climatronic, LMR etc.	35.861,00 €	375,00 €
CUPRA Formentor 1.5 TSI 110kW/150PS 6-Gang inkl. Navigationssystem 10"Display, MAPCARE, Connectivity-Box inkl. Wireless Charger, Parklenkassistent/Rückfahrkamera, Winter-Paket etc.	31.832,00 €	219,00 €
CUPRA Leon Sportstourer 2.0 TSI 180kW/245PS 7-G.-DSG inkl. Climatronic, Vision Plus inkl. Rückfahrkamera/Parklenkassistent, Winter-Paket, Connectivity-Box inkl. Wireless Charger etc.	34.391,00 €	269,00 €
CUPRA Ateca 2.0 TSI 221kW/300PS 7-G.-DSG 4Drive inkl. Bila Weiß, Businesspaket CUPRA, Winter-Paket, Climatronic, Navi, BeatsAudio Soundsystem, Fahrassistenz-Paket, 19" LMR etc.	42.782,00 €	309,00 €
Ford Puma Titanium 5-Türer 1,0l EcoBoost Hybrid 92kW/125PS 6-Gang inkl. Metallic-Lackierung, Navigationssystem, Park-Assistent/Rückfahrkamera, PPS v+h, Winter-Paket, 17" LMR etc.	24.580,00 €	229,00 €
Ford Kuga Titanium 1,5 l EcoBoost 110kW/150PS 6-Gang inkl. Klimaautomatik, Metallic, Navigationssystem inkl. SYNC 3, PPS v+h, Winter-Paket, Heckklappe elektr. + sensorgesteuert etc.	32.773,00 €	319,00 €
Porsche Macan T 195kW/265PS PDK inkl. Panorama Dachsystem, ParkAssistent vorn und hinten inkl. Rückfahrkamera, Spurwechselassistent, Tempolimitanzeige, Apple CarPlay etc.	62.866,00 €	1.149,00 €
Porsche Taycan 280kW/380PS 83,7kWh inkl. Performancebatterie Plus, Wärmepumpe, Range Manager, Spurwechselassistent, ParkAssistent inkl. Rückfahrkamera, SHZ vorne, Ablagenpaket etc.	82.430,00 €	1.149,00 €
SEAT Ateca FR 1.5 TSI ACT 110kW/150PS 7-G.-DSG inkl. Businesspaket NAVIGATION, Parklenkassistent mit Einparkhilfe v+h/Kamera, Winter-Paket, Licht-/Sicht-Paket, Klimaautomatik etc.	32.374,00 €	249,00 €
Skoda Fabia Active 1,0 MPI 48kW/60PS 5-Gang inkl. Klimaanlage, Musiksystem/DAB+, Außenspiegel elektrisch einstell-/beheizbar, LED-Hauptscheinwerfer, Fahrlichtassistent, Speedlimiter etc.	13.563,00 €	109,00 €
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VW Polo Style 1,0 l TSI OPF 70kW/95PS inkl. Klimaanlage, App-Connect für Apple CarPlay und Android Auto, PDC vorn+hinten, Außenspiegel elektr. einstell-/beheizbar, 15" LMR etc.	20.538,00 €	189,00 €
VW T-Cross Style "LW" 1,0 l TSI OPF 81kW/110PS inkl. Navigationssystem, IQ.DRIVE, Design-Paket, Klimaautomatik, Parklenkassistent inkl. Einparkhilfe, Rückfahrkamera, AHK, LMR etc.	28.076,00 €	269,00 €