Formulation of drug delivery systems with patient as well as student centricity

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Cost of non-compliance

Patients want their medications to mesh with their daily lives and regular activities.

Physicians want their patients to maintain strict therapy schedules.

Non-compliance in the US alone was estimated to be as much as $290 billion (*13%* of total annual health care expenditure)!

Report from New England Healthcare Institute (2010)

2

Patient compliance

- **Dosage schedule**
- **Dosage time**
  - **interval**
  - **Before, with, after meals**
- **To avoid interaction (time periods)**
- **Function of the dosage forms**
  (e.g. intact, subdivided if possible)

3

Patient-centric?

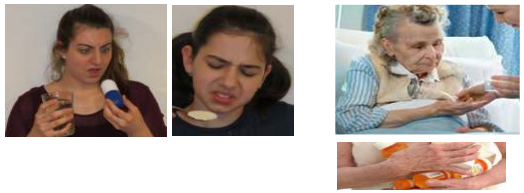
Quality defined by ICH Q9

Although there are a variety of stakeholders including patients and medical practitioners as well as government and industry, **the protection of the patient** by managing the risk to quality should be considered of prime importance.

4

Patient-centric?

ICH Q8: „In all cases, the product should be designed to meet patients' needs and the intended product performance."



Optimization of the
composition, structure, applicability, tolerability and drug delivery of the pharmaceutical dosage form to ensure **tolerability and efficacy**, **and to meet the patient's needs**

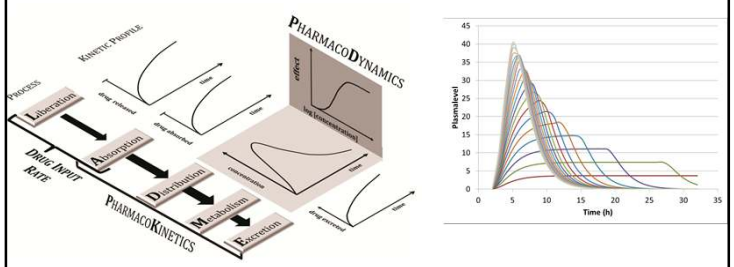
5

Patient-centric drug delivery

- How can Drug Delivery serve patient needs?
- How can Drug Delivery serve patient's pharmacokinetic needs?
- How can Drug Delivery serve patient's individual pharmacokinetic needs?

6

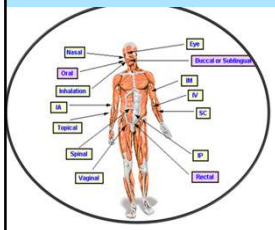
Pharmacokinetic background for DDSs



Stegemann S, Klebovich I, Antal I, Blume H H, Magyar K, Németh G, Paál T L, Stumptner W, Thaler G, Van De Putte A, Shah V P: Improved therapeutic entities derived from known generics as an unexplored source of innovative drug products. EUROPEAN JOURNAL OF PHARMACEUTICAL SCIENCES 44:(4) pp. 447-454. (2011)

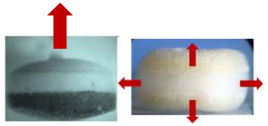
7

Right drug therapy with patient-centric drug delivery



Right route of administration

Right dosage form



Right type of drug release
rate/mechanism (biopharmaceutics)

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Approaches for Drug Delivery Systems

L A D M E

BCS
dissolution
permeability

Targeted delivery, nanocarriers

Drug delivery, alternative dosage forms

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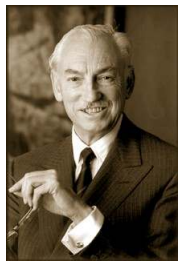
Changing the paradigm in 1960-s for DDSs

Alejandro Zaffaroni
1922 Montevideo
1951 Ph.D (University of Rochester)
1968 ALZA Corp. (Palo Alto, California)
1995 National Medal of Technology.

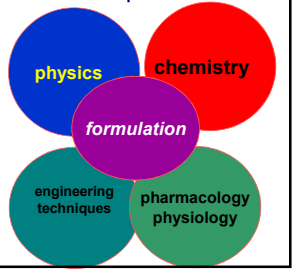
alza — a member of the Johnson & Johnson Company

„The human spirit is always in the search for new ideas."

*„It seemed to me quite evident that **the way in which we administer the agents to the body are wrong**, and if it **is wrong for the hormones, why is it not also wrong for every compound** that we throw all at once into the body?"*



more than 30 products



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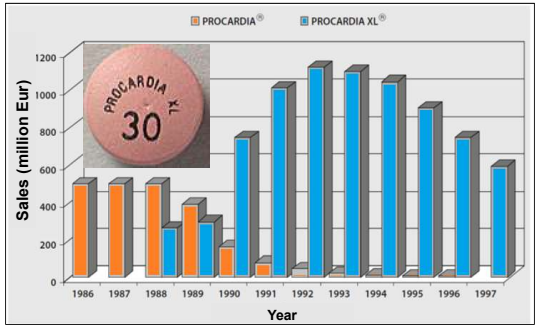
Rediscovery of nifedipine in DDS: the original PK profile led to a blockbuster DDS product



Scrip Magazine May 2000

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New advances in therapy that influence the development of DDSs

- ✓ Chronopharmacology
- ✓ Nanotechnology
- ✓ Biotechnology
- ✓ Pharmacogenetics
- ✓ Pharmacogenomics
- ✓ Pharmacoproteomics
- ✓ Pharmacometabolomics
- ✓ Pharmaceutical care

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Advances in pharmacology that influence the development of DDSs

- ✓ Improved efficacy
- ✓ Improved safety and tolerability
- ✓ Improved patient compliance
- ✓ Chronopharmacological benefits
- ✓ Reduced cost of drug development
- ✓ Extended product lifetime
- ✓ Reduction of risk of failure in new product development

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Drug delivery systems advantages and limitations

Clinical advantages

- ✓ Reduction in frequency of drug administration
- ✓ Improved patient compliance
- ✓ Reduction in drug level fluctuation in blood
- ✓ Reduction in total drug usage when compared with conventional therapy
- ✓ Reduction in drug accumulation with chronic therapy
- ✓ Reduction in drug toxicity (local/systemic)
- ✓ Stabilization of medical condition (because of more uniform drug levels)
- ✓ Improvement in bioavailability of some drugs because of spatial control
- ✓ Economical to the health care providers and the patient

Commercial/industrial advantages

- ✓ Illustration of innovative/technological leadership
- ✓ Product life-cycle extension
- ✓ Product differentiation
- ✓ Market expansion
- ✓ Patent extension

Tiwari SB, Rajabi-Siahboomi AR.: Extended-release oral drug delivery technologies: monolithic matrix systems. Methods Mol Biol. 2008;437:217-43

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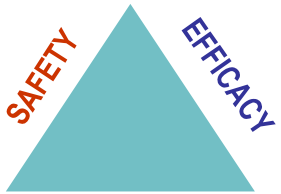
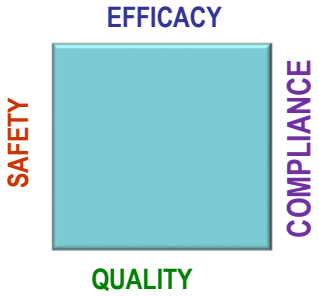
Requirements for the drug therapy

„NIL NOCERE"





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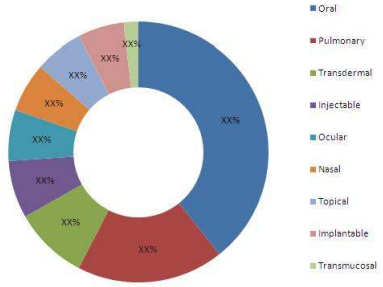
„Drug Delivery Systems"

Drug delivery market:

2013: 160 bn USD
2019: 300 bn USD

Routes

Per os
Pulmonary
Transdermal
Injectable
Ocular
Nasal
Local, topical
Implants
Transmucosal



Forrás: Market and Research

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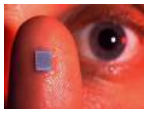
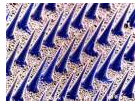
Alternative dosage forms

Buccal films

Inhalation devices

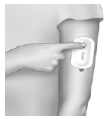
Microfabrication





Iontophoresis ITS (Iontophoretic Transdermal System).

9,7 mg fentanyl
40 ug/10 min



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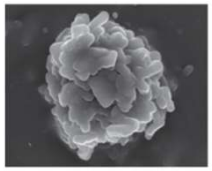
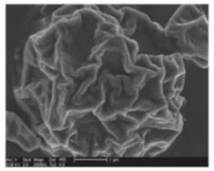
New insulin product for inhalation (2015)

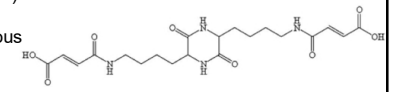




Technosphere® Insulin particle (SEM)

crystalline

amorphous



Matrix: fumaril-diketo-piperazin (FDKP)
soluble at pH>=6
Excreted is unchanged form

Forrás: Mannkind Corp. INNOVATION IN DRUG DELIVERY
BY INHALATION
Angelo R et al. Technosphere® Insulin: Defining the Role of Technosphere Particles at the Cellular Level. J Diabetes Sci Technol. 2009; 3(3): 545–554.

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How to identify the right medicine?

Polypharmacy in older adults
- Elderly take an average of 2 – 6 prescription medicines and 1 – 3 non-prescripion drugs
- 57 % of woman 65 years take ≥ 5 Rx drugs & 12 % ≥ 10 Rx drugs

Visual impairments and poor vision are common in elderly that impact:
- ✓ **Seeing and indentifying the drug products**
- ✓ **Reading medication information**

Poor visual acuity

Good visual acuity

Easy to distinguish	%
White/red	60
Yellow/red	54
White/light blue	52

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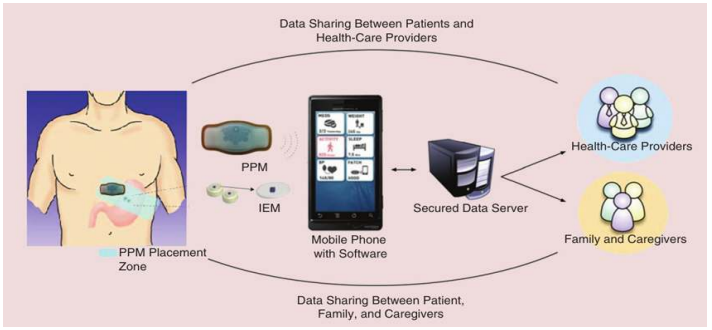
„Proteus Digital Health"

U.S. Patent Number 7,978,064:
"Communication System with Partial Power Source,"



No microchip!
Upon contact with a gastric juice, **the electrolytes of the tablet's coating layer are dissolved and a voltage potential is created as sign.**

http://lifesciences.ieee.org/articles/feature-articles/247-a-digital-health-solution-for-using-and-managing-medications

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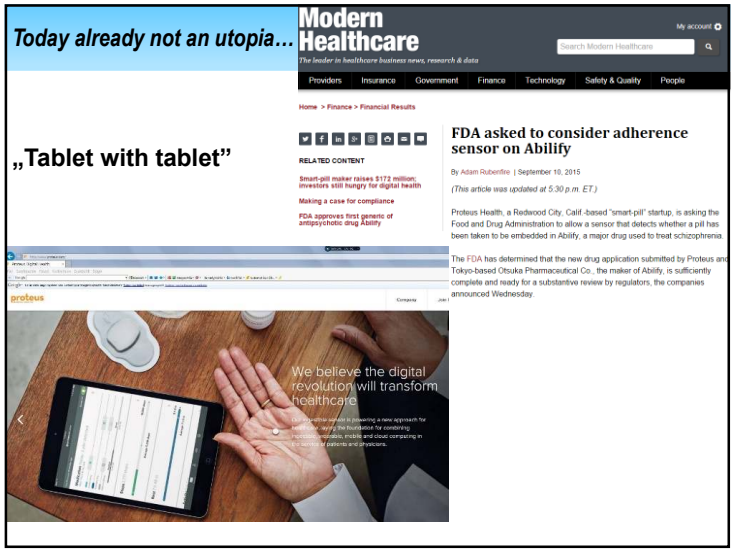
Today already not an utopia…

„Tablet with tablet”



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Patient-centric devices, containers, packaging csomagolás

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Advantage of pellets for swallowing difficulties

prolonged release pellets in capsule

„…Swallow your capsules whole with a glass of water. ***If you prefer, you can open the capsules and sprinkle the contents on to cold soft food****, such as yoghurt. You must only take the capsules by mouth.* ***Do not crush or chew*** *the capsule or the capsule contents…”*

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MUPS for dysphagia…

- Gastroresistant pellet with omeprazole
- Emtying a capsule
- Halving the tablet

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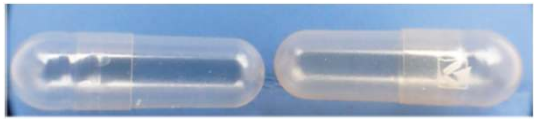
Capsules



Conventional hard gelatine

HPMC capsules (Vcaps)
e.g. for vegeterians)

How important is "vegetarian" in the purchase decision for a Health & Nutrition supplement?
Research, conducted by the Natural Marketing **Institute in 2013, showed that 38% of consumers in the US prefer capsules that are plant-based.** This is a growing trend and up from previous national and global surveys. To receive more detailed information, contact your Customer Service Representative.

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Case study: Gastroretentive DDS

(WO/2009/013552) CONTROLLED RELEASE PHARMACEUTICAL COMPOSITION OF TOLPERISON HYDROCHLORIDE

Biblio. Data | Description | Claims | National Phase | Notices | Documents

Latest bibliographic data on file with the International Bureau

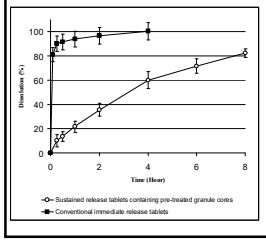
Pub. No.: WO/2009/013552 — International Application No.: PCT/HU2008/000086
Publication Date: 29.01.2009 — International Filing Date: 22.07.2008
IPC: *A61K 9/20* (2006.01), *A61K 31/4453* (2006.01), *A61K 9/50* (2006.01)
Applicants: RICHTER GEDEON NYRT. [HU/HU]; Gyömrői út 19-21, H-1103 Budapest (HU) *(All Except US)*.

(WO/2009/007762) METRONIDAZOLE CONTAINING EXTENDED RELEASE FLOATING PHARMACEUTICAL COMPOSITION

Biblio. Data | Description | Claims | National Phase | Notices | Documents

Latest bibliographic data on file with the International Bureau

Pub. No.: WO/2009/007762 — International Application No.: PCT/HU2008/000081
Publication Date: 15.01.2009 — International Filing Date: 09.07.2008
IPC: *A61K 9/00* (2006.01), *A61K 9/20* (2006.01), *A61K 9/48* (2006.01)
Applicants: RICHTER GEDEON NYRT. [HU/HU]; Gyömrői út 19-21, H-1103 Budapest (HU) *(All Except US)*.



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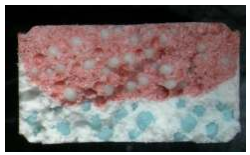
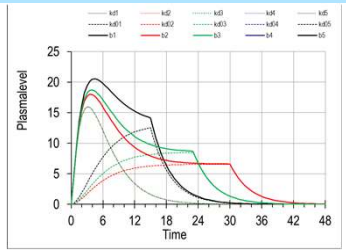
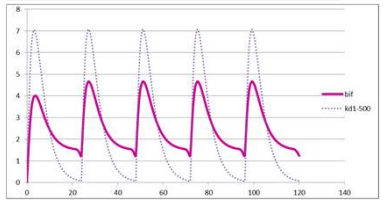
Case study: Multiphase DDS with biphasic drug release (1st and 0-order)







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Case study

ELSEVIER

European Journal of Pharmaceutical Sciences 15 (2002) 157–162

PHARMACEUTICAL SCIENCES
www.elsevier.nl/locate/ejps

In vitro simulation of food effect on dissolution of deramciclane film-coated tablets and correlation with in vivo data in healthy volunteers

Samar Al-Behaisi[a,*], István Antal[b], György Morovján[a], József Szinyog[a], Sándor Drabant[a], Sylvia Marton[a], Imre Klebovich[a]

[a]Research & Development Directorate, EGIS Pharmaceuticals Ltd., Kereszturi ut 30–38, H-1106 Budapest, Hungary
[b]Pharmaceutical Institute, Semmelweis University, Hogyes E. u. 7, 1092 Budapest, Hungary

Received 27 March 2001; received in revised form 30 August 2001; accepted 3 September 2001

Abstract

The in vitro dissolution profiles of deramciclane 30 mg film-coated tablets, an acid-labile new 5-HT receptor antagonist, were studied under simulated fasting and fed conditions. Artificial gastric juice with pH adjusted to that of fasting conditions was applied either alone or after adding different dietary components. The use of the USP dissolution apparatus II (paddle method) showed that the presence of dietary components has markedly affected the amount of unchanged drug dissolved. As a similar tendency had been observed in food-effect studies in healthy volunteers, cumulative area under the curve (AUC_{max}) for both fed and fasting conditions were compared and an in vitro–in vivo correlation (IVIVC) was evaluated. A linear relationship was established between logarithmic in vivo blood sampling time and in vitro dissolution time assigned to equal AUC_{max} ratios ($AUC_{max,\ fed}/AUC_{max,\ fasting}$). Despite its limitations, in vitro modelling of in vivo conditions might help provide a base for predicting in vivo drug behaviour. © 2002 Published by Elsevier Science B.V.

Keywords: Deramciclane; Dissolution; Food effect; AUC_{max}; In vitro–in vivo correlation

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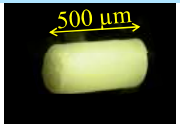
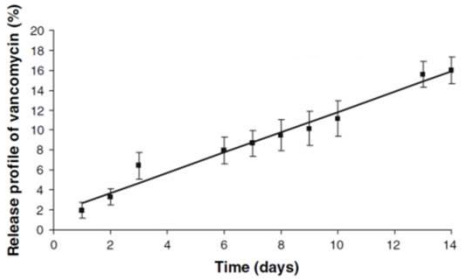
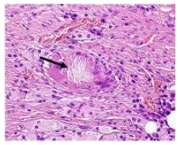
Multiunit DDS for orthopaedic surgery

vancomycin containing waxy carrier systems that release the antibiotic over a prolonged period (2-8 weeks) .



melt extruded sticks





biodegradation by phagocytosis

Laki M, Hajdú M, Ludányi K, Zahár Á, Szendroi M, Klebovich I, Antal I: Evaluation of a new LC method for analysis of vancomycin released from an orthopaedic drug carrier system. Chromatographia 68: 141-144. (2008)

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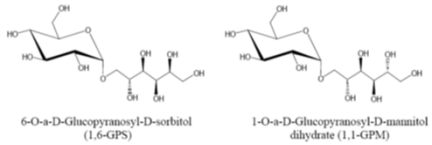
Case study for key formulation factors: coated layered pellets

Isomalt (galenIQ® 980 and 981)



- **sugar free**
- **low hygroscopicity**
- ***low compatibility***
- ***no additives for the production***

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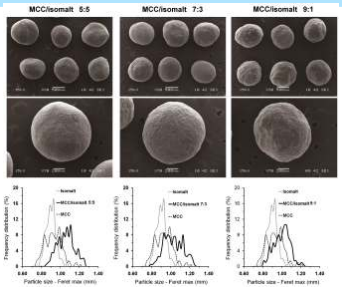
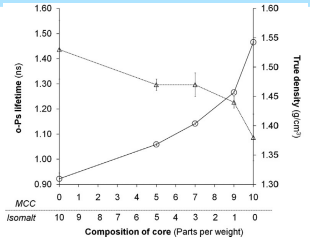
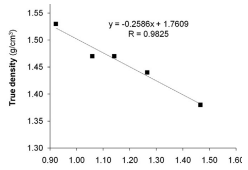
Case study for key formulation factors: composite pellet core







A physical interaction was found between the microcrystalline cellulose and isomalt which supports the osmotic effect of the water soluble sugar alcohol in the composite pellet cores regarding drug release.

Antal I, Kállai N, Luhn O, Bernard J, Nagy ZK, Szabó B, Klebovich I, Zelkó R.: Supramolecular elucidation of the quality attributes of microcrystalline cellulose and isomalt composite pellet cores. J Pharm Biomed Anal. 84:124-8 (2013)

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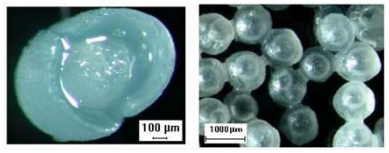
Case study for key formulation factors: coated layered pellets
Dissolution study with simulation of osmotic effect in the GIT

The effect of the osmolality in the GIT was simulated using glucose as osmotically active agent during in vitro dissolution tests in pH=6.8 phosphate buffer:

0.106 Osmol/kg
0.483 Osmol/kg
0.706 Osmol/kg



1 hour 24 hours

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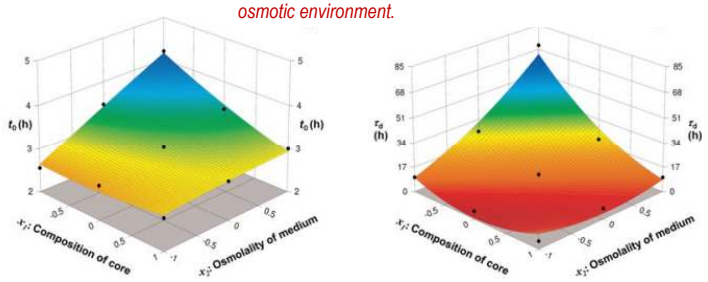
Case study for key formulation factors: composite pellet core

Isomalt used in the composite core was able to decrease the vulnerability of the dissolution kinetics to the changes in the osmotic environment.



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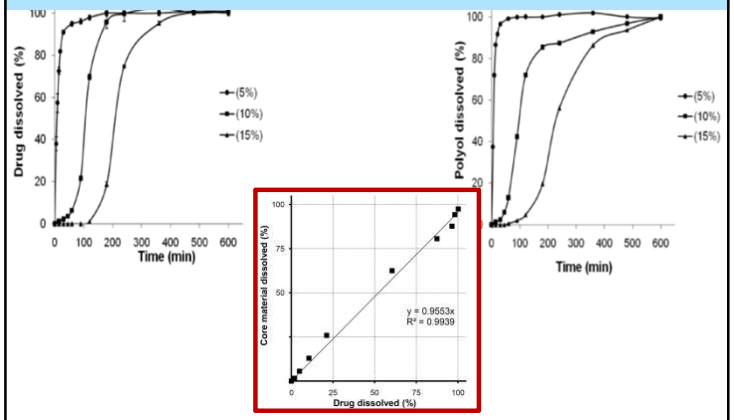
Case study for key formulation factors: coated layered pellets



Kállai-Szabó N., Luhn O., Bernard J., Kállai-Szabó B., Zelkó R., Antal I.: Comparative dissolution study of drug and inert isomalt based core material from layered pellets, J. Pharm. Biomed. Anal., in press

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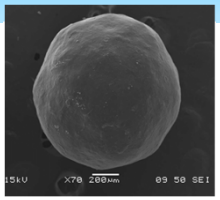
Case study for key formulation factors: coated layered pellets

Objective

Evaluating the commercial inert pellet cores and to develope starter pellets composed from both microcrystalline cellulose (MCC) and isomalt.



Manufacture

The pellet cores were manufactured by an ***extrusion/spheronisation*** process and their most important characteristics were compared to pure isomalt cores and to the commonly used MCC-based inert spheres. MCC/isomalt cores were layered with a poorly water soluble drug (sodium diclofenac) and were coated with acrylic polymer.

Tests:

physical quality attributes (size and size distribution, spherical shape, mechanical strength)

drug release profile, sensitivity to osmotic pressure

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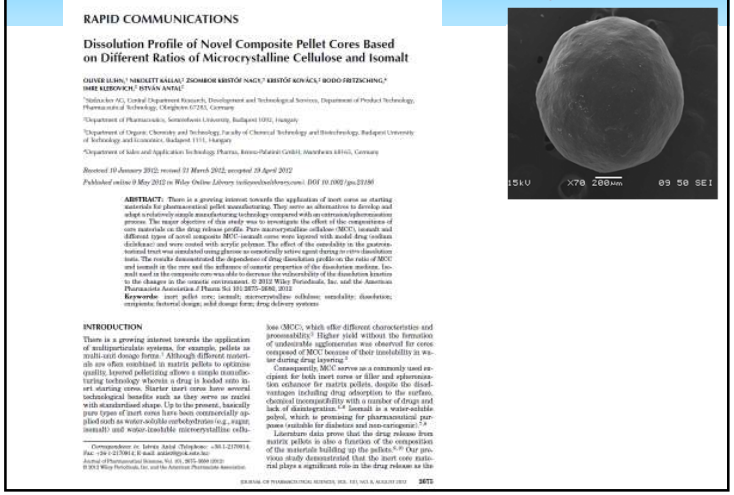
Case study for key formulation factors: coated layered pellets



RAPID COMMUNICATIONS

Dissolution Profile of Novel Composite Pellet Cores Based on Different Ratios of Microcrystalline Cellulose and Isomalt

OLIVER ULBIN,[1] NIKOLETT KÁLLAI,[2] ZSOMBOR KRISTÓF NAGY,[3] KRISTÓF KOVÁCS,[3] BODO FRITZSCHING,[4] IMRE KLEBOVICH,[2] ISTVÁN ANTAL[2]

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ABSTRACT: There is a growing interest towards the application of inert cores as starting materials for pharmaceutical pellet manufacturing. They serve as alternatives to develop and adopt a relatively simple manufacturing technology compared with an extrusion/spheronization process. The major objectives of this study was to investigate the effect of the compositions of core materials on the drug release profile. Pure microcrystalline cellulose (MCC), isomalt and different types of novel composite MCC-isomalt cores were layered with model drug (sodium diclofenac) and were coated with acrylic polymer. The effect of the osmolality in the gastrointestinal tract was simulated using glucose as osmotically active agent during in vitro dissolution tests. The results demonstrated the dependence of drug dissolution profile on the ratio of MCC and isomalt in the core and the influence of osmotic properties of the dissolution medium. Isomalt used in the composite cores was able to decrease the vulnerability of the dissolution kinetics to the changes in the osmotic environment. © 2012 Wiley Periodicals, Inc. and the American Pharmacists Association *J Pharm Sci* 101:2675–2686, 2012

Keywords: inert pellet core; isomalt; microcrystalline cellulose; osmolality; dissolution; excipients; factorial design; solid dosage form; drug delivery systems

INTRODUCTION

There is a growing interest towards the application of multiparticulate systems, for example, pellets as multi-unit dosage forms.[1] Although different materials are often combined in matrix pellets to optimize quality, layered pelletizing allows a simple manufacturing technology wherein a drug is loaded onto inert starting cores. Starter inert cores have several technological benefits such as they serve as nuclei with standardised shape. Up to the present, basically pure types of inert cores have been commercially applied such as water-soluble sugar spheres (e.g., sugar, isomalt) and water-insoluble microcrystalline cellulose (MCC), which offer different characteristics and processability.[2] Higher yield without the formation of undesirable agglomerates was observed for cores composed of MCC because of their insolubility in water during drug layering.[3]

Consequently, MCC serves as a commonly used excipient for both inert cores or filler and spheronization enhancer for matrix pellets, despite the disadvantages including drug adsorption to the surface, chemical incompatibility with a number of drugs and lack of disintegration.[4–6] Isomalt is a water-soluble polyol, which is promising for pharmaceutical purposes (suitable for diabetics and non-cariogenic).[7–9]

Literature data prove that the drug release from matrix pellets is also a function of the composition of the materials building up the pellets.[9–11] Our previous study demonstrated that the inert core material plays a significant role in the drug release as the

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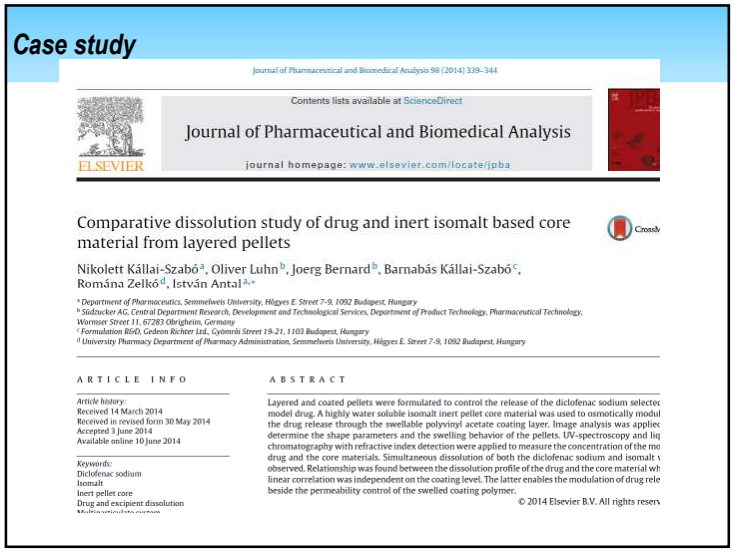
Case study



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Comparative dissolution study of drug and inert isomalt based core material from layered pellets

Nikolett Kállai-Szabó[a], Oliver Luhn[b], Joerg Bernard[b], Barnabás Kállai-Szabó[c], Romána Zelkó[d], István Antal[a,*]

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Diclofenac sodium
Isomalt
Inert pellet core
Drug and excipient dissolution

ABSTRACT

Layered and coated pellets were formulated to control the release of the diclofenac sodium selected model drug. A highly water soluble isomalt inert pellet core material was used to osmotically modul the drug release through the swellable polyvinyl acetate coating layer. Image analysis was applied determine the shape parameters and the swelling behavior of the pellets. UV-spectroscopy and liq chromatography with refractive index detection were applied to measure the concentration of the mo drug and the core materials. Simultaneous dissolution of both the diclofenac sodium and isomalt observed. Relationship was found between the dissolution profile of the drug and the core material wh linear correlation was independent on the coating level. The latter enables the modulation of drug rele beside the permeability control of the swelled coating polymer.

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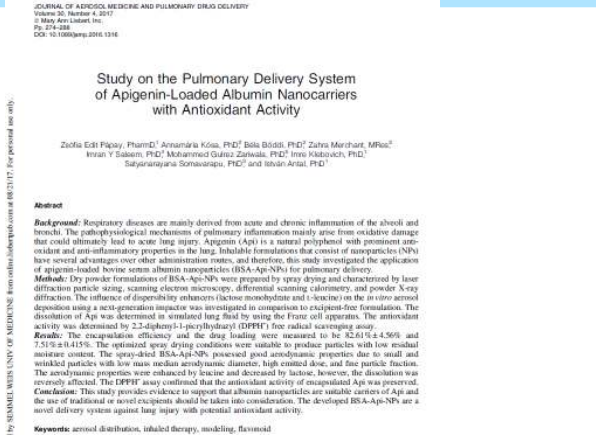
Case study



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Study on the Pulmonary Delivery System of Apigenin-Loaded Albumin Nanocarriers with Antioxidant Activity

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Abstract

Background: Respiratory diseases are mainly derived from acute and chronic inflammation of the alveoli and bronchi. The pathophysiological mechanisms of pulmonary inflammation mainly arise from oxidative damage that could ultimately lead to acute lung injury. Apigenin (Api) is a natural polyphenol with prominent anti-oxidant and anti-inflammatory properties in the lung. Inhalable formulations that consist of nanoparticles (NPs) have several advantages over other administration routes, and therefore, this study investigated the application of apigenin-loaded bovine serum albumin nanoparticles (BSA-Api-NPs) for pulmonary delivery.
Methods: Dry powder formulations of BSA-Api-NPs were prepared by spray drying and characterized by laser diffraction particle sizing, scanning electron microscopy, differential scanning calorimetry, and powder X-ray diffraction. The influence of dispersibility enhancers (lactose monohydrate and L-leucine) on the *in vitro* aerosol deposition using a next-generation impactor was investigated in comparison to excipient-free formulation. The dissolution of Api was determined in simulated lung fluid by using the Franz cell apparatus. The antioxidant activity was determined by 2,2-diphenyl-1-picrylhydrazyl (DPPH•) free radical scavenging assay.
Results: The encapsulation efficiency and the drug loading were measured to be 82.61 % ± 4.56% and 7.51 % ± 0.415%. The optimized spray drying conditions were suitable to produce particles with low residual moisture content. The spray-dried BSA-Api-NPs possessed good aerodynamic properties due to small and wrinkled particles with low mass median aerodynamic diameter, high emitted dose, and fine particle fraction. The aerodynamic properties were enhanced by leucine and decreased by lactose, however, the dissolution was reversely affected. The DPPH• assay confirmed that the antioxidant activity of encapsulated Api was preserved.
Conclusion: This study provides evidence to support that albumin nanoparticles are suitable carriers of Api and the use of traditional or novel excipients should be taken into consideration. The developed BSA-Api-NPs are a novel delivery system against lung injury with potential antioxidant activity.

Keywords: aerosol distribution, inhaled therapy, modeling, flavonoid

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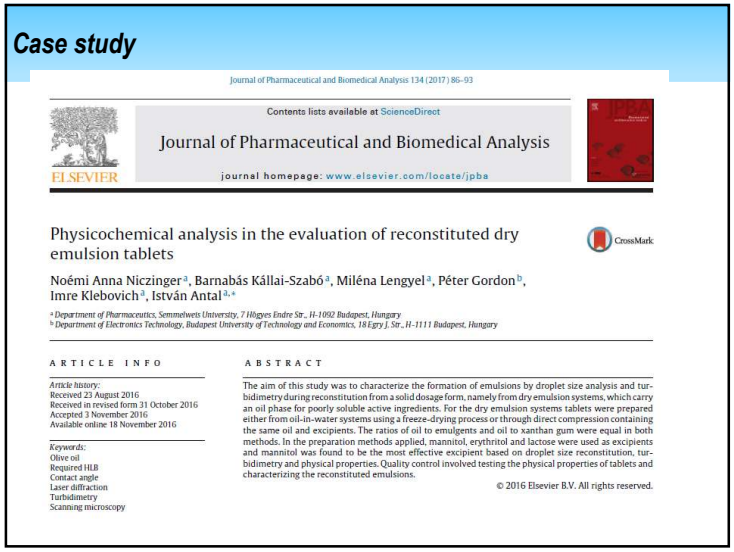
Case study



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Physicochemical analysis in the evaluation of reconstituted dry emulsion tablets

Noémi Anna Niczinger[a], Barnabás Kállai-Szabó[a], Miléna Lengyel[a], Péter Gordon[b], Imre Klebovich[a], István Antal[a,*]

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Olive oil
Required HLB
Contact angle
Laser diffraction
Turbidimetry
Scanning microscopy

ABSTRACT

The aim of this study was to characterize the formation of emulsions by droplet size analysis and turbidimetry during reconstitution from a solid dosage form, namely from dry emulsion systems, which carry an oil phase for poorly soluble active ingredients. For the dry emulsion systems tablets were prepared either from oil-in-water systems using a freeze-drying process or through direct compression containing the same oil and excipients. The ratios of oil to emulgents and oil to xanthan gum were equal in both methods. In the preparation methods applied, mannitol, erythritol and lactose were used as excipients and mannitol was found to be the most effective excipient based on droplet size reconstitution, turbidimetry and physical properties. Quality control involved testing the physical properties of tablets and characterizing the reconstituted emulsions.

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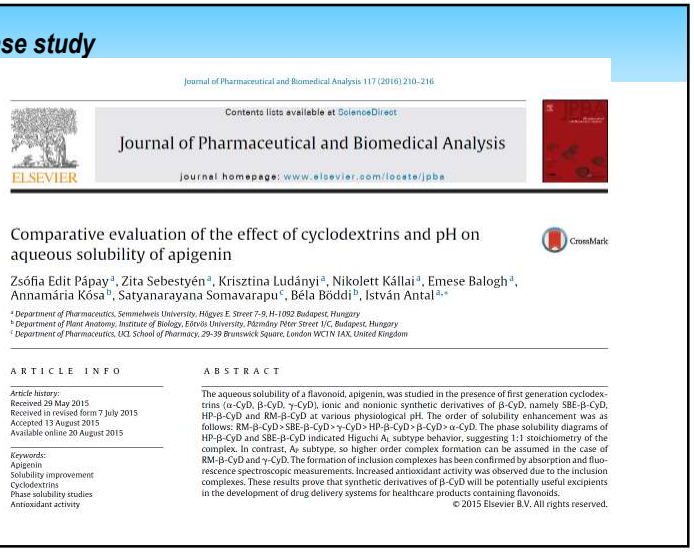
Case study



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Comparative evaluation of the effect of cyclodextrins and pH on aqueous solubility of apigenin

Zsófia Edit Pápay[a], Zita Sebestyén[a], Krisztina Ludányi[a], Nikolett Kállai[a], Emese Balogh[a], Annamária Kósa[b], Satyanarayana Somavarapu[c], Béla Böddi[b], István Antal[a,*]

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Apigenin
Solubility improvement
Cyclodextrins
Phase solubility studies
Antioxidant activity

ABSTRACT

The aqueous solubility of a flavonoid, apigenin, was studied in the presence of first generation cyclodextrins (α-CyD, β-CyD, γ-CyD), ionic and nonionic synthetic derivatives of β-CyD, namely SBE-β-CyD, HP-β-CyD and RM-β-CyD at various physiological pH. The order of solubility enhancement was as follows: RM-β-CyD > SBE-β-CyD > γ-CyD > HP-β-CyD > β-CyD > α-CyD. The phase solubility diagrams of HP-β-CyD and SBE-β-CyD indicated Higuchi A_L subtype behavior, suggesting 1:1 stoichiometry of the complex. In contrast, A_P subtype, so higher order complex formation can be assumed in the case of RM-β-CyD and γ-CyD. The formation of inclusion complexes has been confirmed by absorption and fluorescence spectroscopic measurements. Increased antioxidant activity was observed due to the inclusion complexes. These results prove that synthetic derivatives of β-CyD will be potentially useful excipients in the development of drug delivery systems for healthcare products containing flavonoids.

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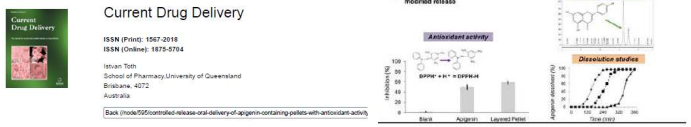
Case study



Current Drug Delivery

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Back (/node/595/controlled-release-oral-delivery-of-apigenin-containing-pellets-with-antioxidant-activity)

Controlled release oral delivery of apigenin containing pellets with antioxidant activity

Author(s): Zsófia Edit Pápay, Nikolett Kállai-Szabó, Emese Balogh, Krisztina Ludányi, Imre Klebovich and István Antal

Affiliation: Department of Pharmaceutics of the Semmelweis University, Hogyes Endre Str. 7, 1092 Budapest, Hungary.

Abstract:

Background: Drug delivery of phytochemicals has gained interest recently due to their remarkable health effects. Apigenin, a plant flavonoid, has antioxidant, anti-inflammatory and anticancer activities but its delivery is challenging. It could be absorbed through the whole intestine, however, it has poor bioavailability due to its low aqueous solubility. In Europe, the daily intake was estimated to be as low as 2±1 mg. Pellets offer several advantages such as improved bioavailability and various resultant drug release profiles can be obtained by simply mixing pellets with different coatings. Objective: The objective of our study was to develop a carrier system containing 20 mg apigenin thus enhancing intake and to offer reduction of oxidative stress which can cause inflammation in the intestine. Method: The apigenin powder was dispersed in aqueous solution of binding material and layered onto the inert cores in a fluidized bed apparatus. The layered cores were further coated with enteric polymers and the process parameters were optimized. Results: The prepared pellets met with the requirements and have good physical characteristic. 10 % (w/w) Eudragit® L was suitable for enteric coating with a complete release at pH 6.8 within 1 hour. 15% (w/w) Eudragit® FS coating ensured acid resistance ability and colonic delivery. The therapeutic efficiency was confirmed with antioxidant activity measurement by using DPPH• assay. Conclusion: Enteric coated spheres allow targeted delivery into the intestine and colon thus reaching the main absorption site. Pellets were proved to be an optimal delivery system for apigenin thus providing enhanced apigenin intake.

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Case study

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Current Pharmaceutical Analysis, 2015, 11, 11-15 11

Application of Droplet Size Analysis for the Determination of the Required HLB of Lemon Oil in O/W Emulsion

N.A. Niczinger, N. Kállai-Szabó, J. Dredán, L. Budai, M. Hajdú and I. Antal*

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Abstract: Hydrophile-lipophile balance method is one of the requirements which can complete the existing guidelines, thereby making the most stable emulsion. The aim of present work was to determine the required hydrophile-lipophile balance of lemon essential oil in oil-in-water emulsions. Paraffin oil and its known required hydrophile-lipophile balance were used as a standard. Span 80 and Tween 80 or Gelucire 44/14 blend were applied as emulsifying agents. Emulsions were evaluated by droplet size distribution and turbidity measurements. Based on the estimated stability of emulsion series and according to the droplet size analysis with lower variations, the required hydrophile-lipophile balance of lemon oil was measured approximately 12 in oil-in-water systems.

Keywords: Droplet size distribution, oil-in-water emulsion, paraffin oil standard, required HLB, surface active agents, turbidity.

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Case study

Polymer Testing 32 (2013) 1322–1325

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Material characterisation

Structural elucidation of hyaluronic acid gels after heat sterilisation

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Hyaluronic acid
Hydrogel
Heat sterilisation
Positron annihilation lifetime spectroscopy

ABSTRACT

The influence of heat sterilisation and hyaluronic acid (HA) concentration on the micro- and macrostructure of HA hydrogels was investigated. HA hydrogels of different concentrations were prepared and heat sterilised. The microstructures of the polymer gels were characterised by positron annihilation lifetime spectroscopy (PALS) based on their ortho-positronium lifetime values and distributions, while their macrostructures were characterised by rheological measurements. As expected, the heat sterilisation modified both the micro- and macrostructures of the gels. The HA concentration was also observed to influence the hydrogel structure. At a concentration of 7.5 mg/ml HA, the thermal treatment did not cause significant microstructural changes, and the viscoelastic properties of the treated gels were similar to those of the untreated samples.

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Case study

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Microstructural analysis of the fast gelling freeze-dried sodium hyaluronate

Andrea Krüger-Szabó[a], Zoltán Aigner[b], Emese Balogh[c], István Sebe[d], Romána Zelkó[d], István Antal[c,*]

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Sodium hyaluronate (NaHA)
Freeze-drying
Fast gelling
Viscoelasticity
Positron annihilation lifetime spectroscopy

ABSTRACT

Although sodium hyaluronate is a very unstable and heat sensitive molecule, it can remain relatively stable during the freeze-drying process. Aqueous sodium hyaluronate (NaHA) gels were prepared and the obtained samples were freeze-dried. The freeze-dried NaHA samples showed fast gelling ability meanwhile preserved their initial viscoelasticity even after reconstitution. The microstructure of gels obtained from raw substance and freeze-dried NaHA samples was characterized with positron annihilation lifetime spectroscopy and X-ray diffraction patterns while their functionality-related macrostructural properties were tested based on their rheological behavior. The presence of phosphate salts improved the formation of ordered supramolecular structure retaining water in the free volume holes of the polymer chains characterized with decreased ortho-positronium lifetime values. This property may be advantageous in the development of a freeze-dried NaHA injection dosage form.

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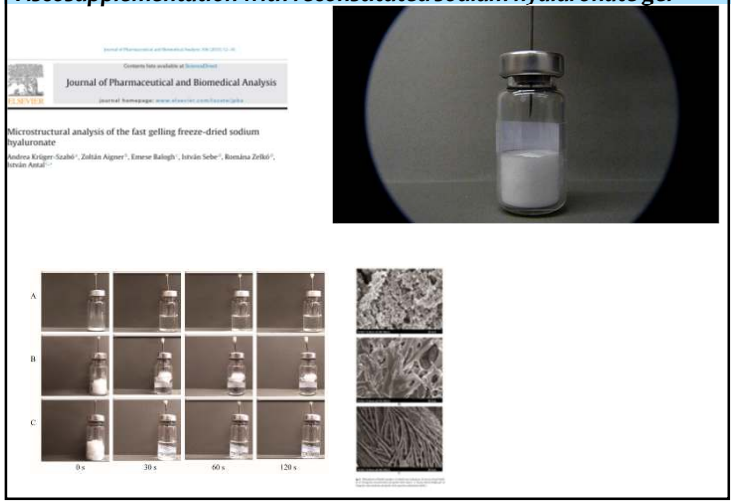
Case study:
Viscosupplementation with reconstituted sodium hyaluronate gel



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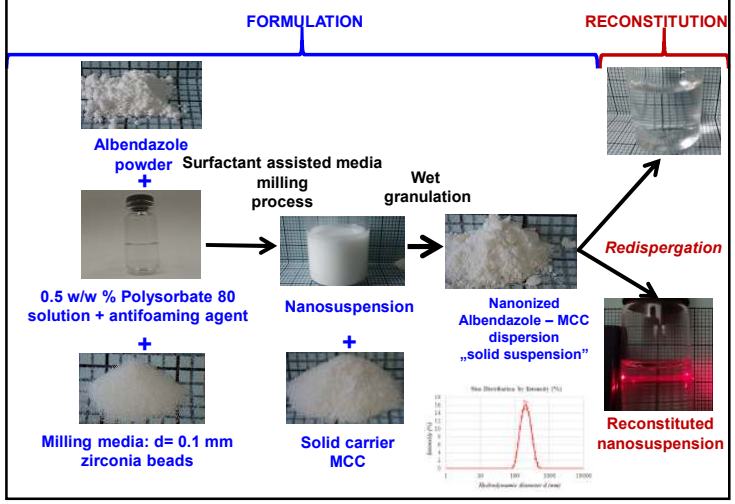
Study on dissolution of albendazole improved by reconstitutable dry nanosuspension
Viktor Fülöp, Géza Jakab, Bence Tóth, Dániel Endrésik, Emese Balogh, István Antal



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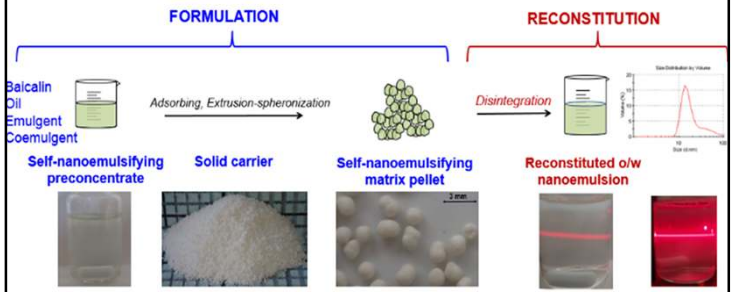
Formulation and investigation of baicalin in liquid and solid Self-nano emulsifying Drug Delivery Systems
Jakab G., Fülöp V., Szerőczei D., Aghrabi E., Balogh E., Antal I.



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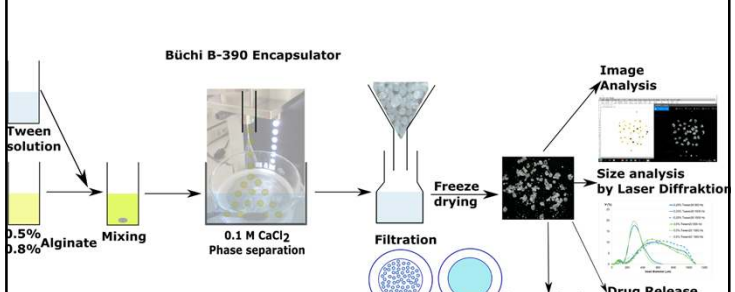
Study on the effect of surfactants and optimization of process parameters of the microencapsulation based on phase separation
Lengyel, M., Stömmer, V., Szerőczei, D., Bertalanné Balogh, E., Klebovich, I., Antal, I.



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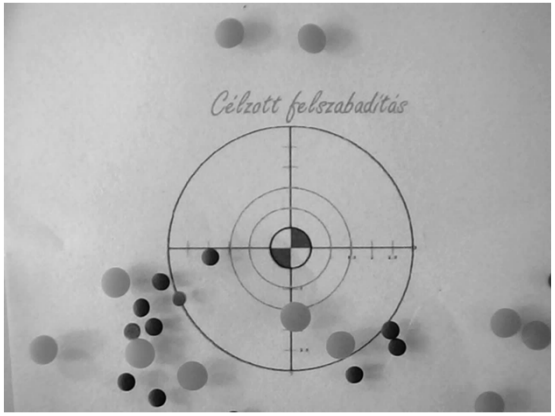
Magnetic sensitive alginate microbeads



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Summary

- patient centric drug delivery systems offer improved effectiveness and tolerability,
- controlled drug release can be due to special structure (composition/manufacturing technology) and properties of the dosage forms,
- drug delivery may help the effectiveness and tolerability

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Student centric?

- ✓ **actual topic research**
- ✓ **interesting ideas**
- ✓ **motivating formulation**
- ✓ **time…**

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*"**The known is finite, the unknown infinite**; **intellectually we stand on an islet** in the midst of an illimitable ocean of inexplicability. Our business in every generation is to reclaim a little more land, to add something to the extent and the solidity of our possessions."*

Thomas Henry Huxley
4 May 1825 – 29 June 1895

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Many thanks…


Samer Al-Behaisi (2002) — *Chief Medical Officer and Vice President of Medical Affairs at Race Oncology Ltd, Melbourne*


Zoltán Bozoky (2004) — *Frédéric Joliot-Curie" Research Institute. for Radiobiology and Radiohygiene, Budapest*


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Zsófia Sáska (2013) — *Gedeon Richter PLC., Budapest*


Andrea Krüger Szabó (2015) — *LEO Pharma, Denmark/Germany*


Zsófia Pápay (2017) — *coworker*


Noémi Niczinger (2018) — *coworker*

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