

Basic Concepts of Oral Drug Delivery: What You Need To Know

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Basic Concepts of Oral Drug Delivery: What You Need To Know

*What I wish I knew when I started many years ago and paid the price for not knowing**



'Unexpected': Breast Cancer Spreads Most During Sleep

Megan Brooks

June 28, 2022



67



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New research shows that the metastatic spread of [breast cancer](#) occurs predominantly during sleep, a discovery the investigators called "striking and unexpected."

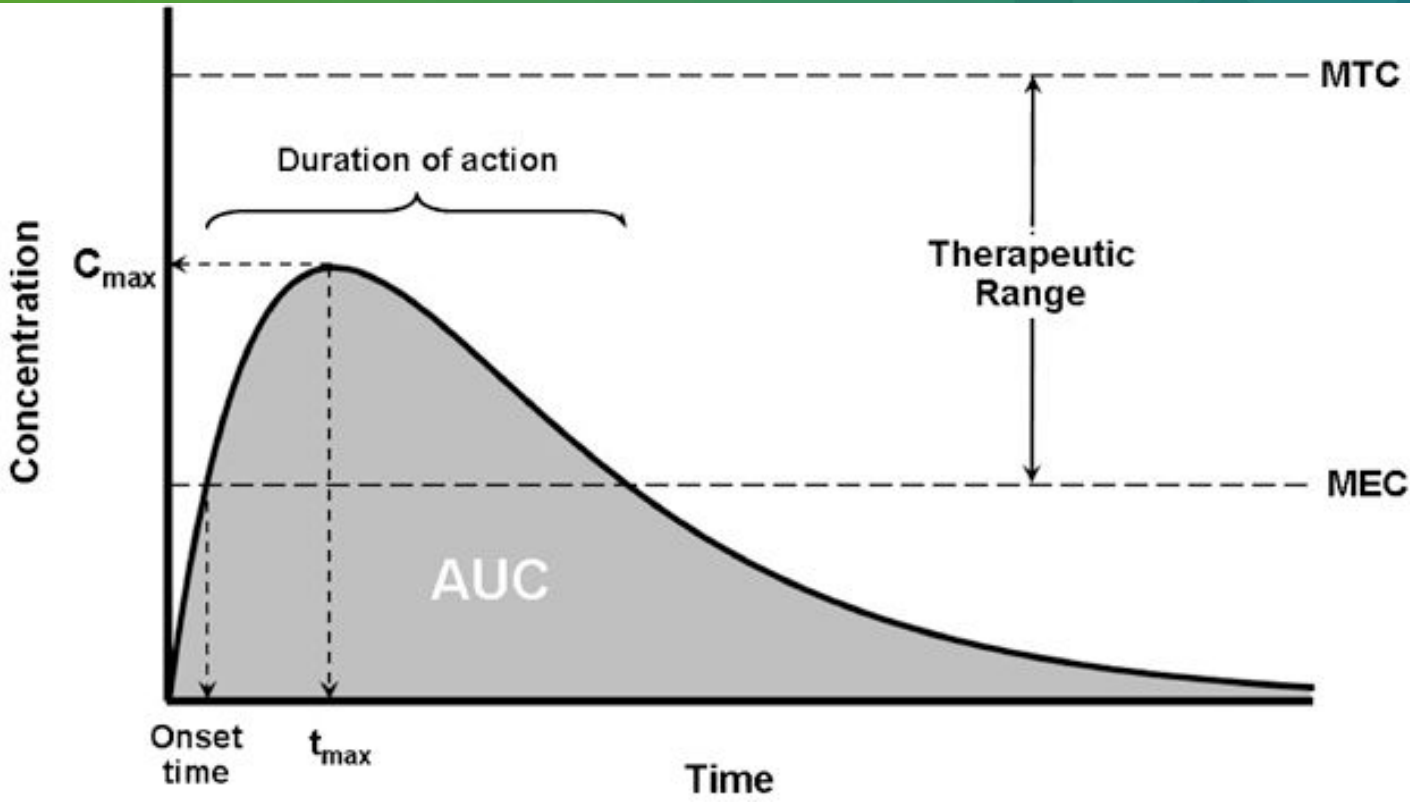
"This has not been shown before [and] we were surprised, indeed," Nicola Aceto, PhD, professor of molecular oncology, Swiss Federal Institute of Technology (ETH) Zurich, Switzerland, told *Medscape Medical News*.

The findings carry potential implications for the timing of biopsy and treatment

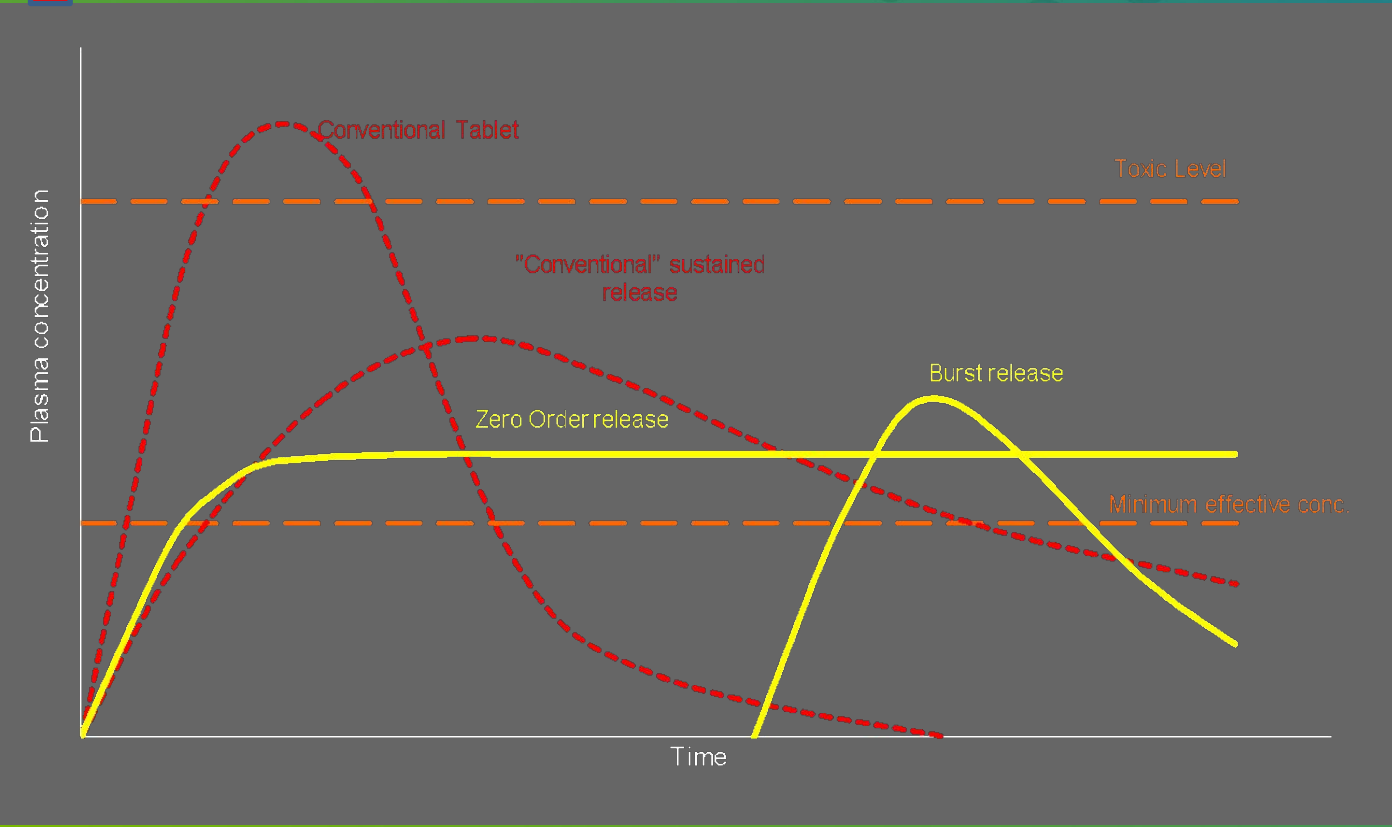
ADME – LADME - *In Vivo In Vitro* Correlation – Dissolution Testing – Compendial Methods – Regulatory requirements – Material sciences – GRASE ingredients – Pharmacopoeia monograph – Gastrointestinal physiology – Patents – Manufacturing processes – Pharmacokinetics – Pharmacodynamics – Patient compliance – Swallowing – Organoleptics – Bioadhesion – Transporters – Window of absorption – Imaging - Clinical trial – Bioequivalence – NDA – NCI – ANDA – FDA – EMA – Batch – Toxicology – Novel ingredients – Instrumentation suppliers – Raw materials suppliers – *In Silico* models – Pharmacokinetic profiles – Toxicological considerations – Adverse effects – Transit time(s) – Residence times – Bezoar – Particle size – Crystallinity – Solubility – Rate of dissolution – Amorphous state – Particle engineering – Molecular dispersion – Suspensions – Granulation – Coating – Encapsulation – Coacervation – Hollow fibres – Spinning – Thermoplastics – Calendering - Extruding – Injection moulding – Spheronization – Pellets – Calibration curve – HPLC – XRPD – DSC – Release profiles – Stability – Shelf life – Packaging – Genetics – Cultural factors – CROs – Consultants – GMP – GLP – Chylomicrons – Lymphatic pathway – First-pass metabolism - Blood Brain Barrier – Co-crystals – Dendrimers – Liposomes – Hepatic recirculation – Microbiome – Available water – Regional pH – Inter-individual variation – Intra-individual variation – Superiority – Nano-size – Diffusion – Erosion – Polymers – Targets - Clinical significance – Smartphones – 3D printing – Inkjet printing – Microwaves, Analytical methods, Surfaces, CACO-2, PAMPA, Animal models AND a lot more



ADME – Immediate Release, I.R.



LADME (“L” for Liberation)



What are you talking about?

- Controlled Release
- Modified Release
- Continuous Release
- Extended Release
- Sustained Release
- Depot
- Delayed Release
- Burst Release
- Delayed Burst Release



Doctor writes, patient reads...

q.d. "quaque die", in Latin, (once) every day

b.i.d. "bis in die", in Latin, twice a day

t.i.d. "ter in die", in Latin, 3 times a day

q.i.d. "quater in die", in Latin, 4 times a day

q_h: "quaque hora" in Latin, every so many hours, "h" indicating the number of hours

Let's start with the exception (1953!)

NDC 0149-0008-05
LIST 70805

50 mg

Macrodan[®]
(nitrofurantoin
macrocrystals)

Avoid excessive heat (over 104°F or 40°C).
**THIS IS A BULK CONTAINER AND
NOT INTENDED FOR DISPENSING.**
Dispense in a tight container.

**URINARY TRACT
ANTIBACTERIAL
100 Capsules**

CAUTION: Federal law
prohibits dispensing
without prescription.

Norwich Eaton

DOSAGE: Adults: 50 to 100 mg
q.i.d. with food.
See package insert for indications,
precautions, and dosage.

Manufactured by Eaton Laboratories, Inc.
Manatí, Puerto Rico 00701
Distributed by
Norwich Eaton Pharmaceuticals, Inc.
A Procter & Gamble Company © 1964 NEPh
Norwich, New York 13815 00805-L5



Modifying Drug Delivery: *Delayed Release - I*



Chattanooga Times Free Press Bennett

CRS

Leading
Delivery Science
and Technology

Modifying Drug Delivery: *Delayed Release - II*



**EXPECT
DELAYS
AHEAD**



Delay or DELAY?

IMAGINE IF YOU COULD LAST 5 - 10 TIMES LONGER
ENJOY LONGER LASTING SEX



DELAY HELPS YOU TO PROLONG THE PENETRATION TIME AND
GIVES YOU TOTAL CONTROL OVER WHEN YOU EJACULATE.

- ⚡ Delays and controls ejaculation time.
- ⚡ Promotes stronger and firmer erections.
- ⚡ Increases sexual libido and stamina.
- ⚡ 100% Natural Product.

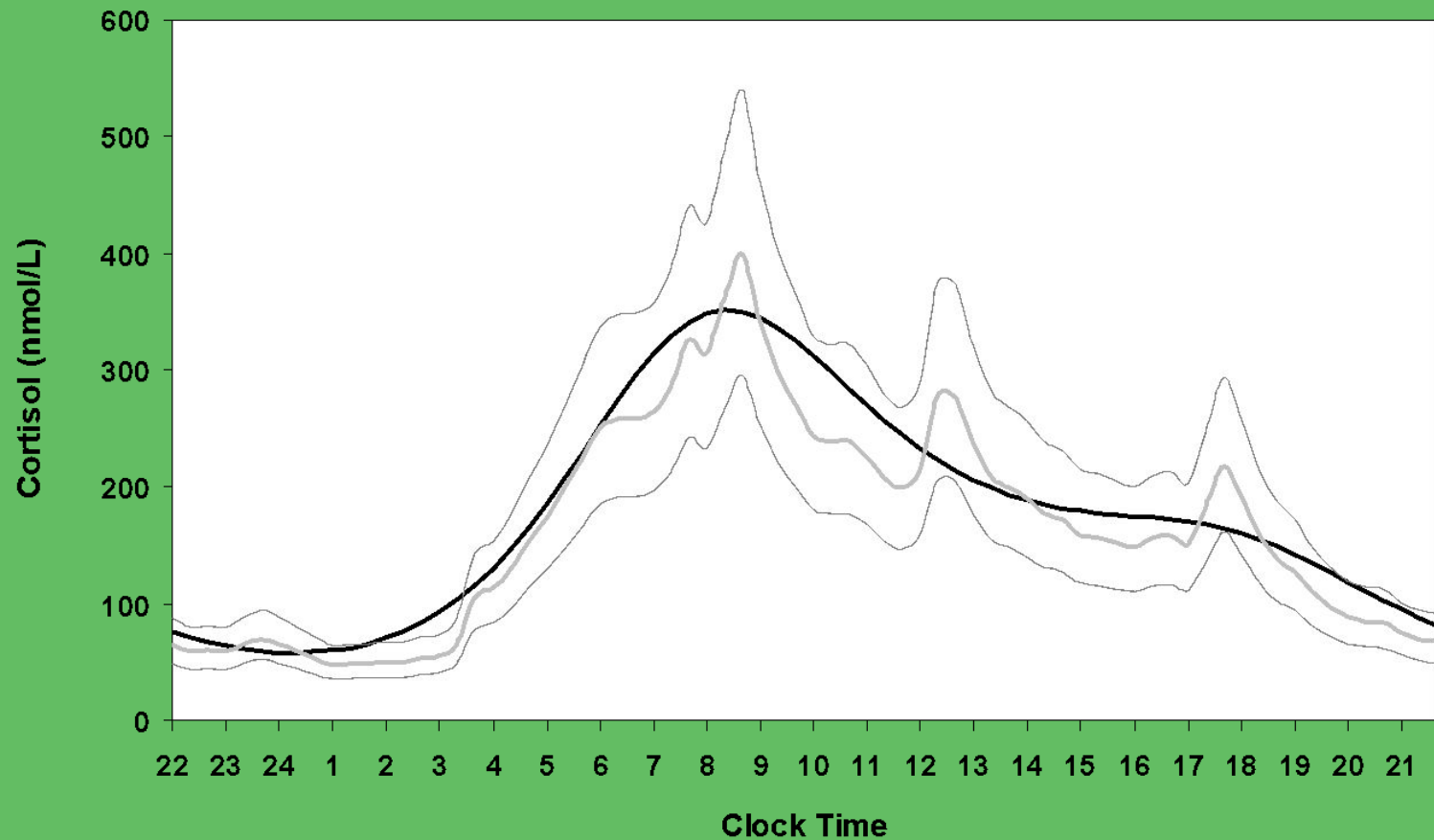
Order Now



Chronotherapy

Addison's disease





Newell-Price J, Whiteman M, Rostami-Hodjegan A, Darzy K, Shalet S, Tucker GT, Ross RJM. Modified-release hydrocortisone for circadian therapy: a proof-of-principle study in dexamethasone-suppressed normal volunteers. *Clinical Endocrinology* 68, 130–135 (2008).

<http://clasfaculty.ucdenver.edu/callen/1202/Landscapes/KarCoast/Coastal/CoastalLandscapes.htm>



Erosion - I



Erosion – Constant Release

A 3D rendering of a green, cylindrical tablet. The top surface of the tablet is white and shows a semi-circular, eroded shape, representing the constant release of a substance from the tablet. The tablet is positioned diagonally within a dark gray rectangular area.

Original Animation by Edward Sharf

Erosion – Delayed Burst Release



Original Animation by Edward Sharf

Erosion - II

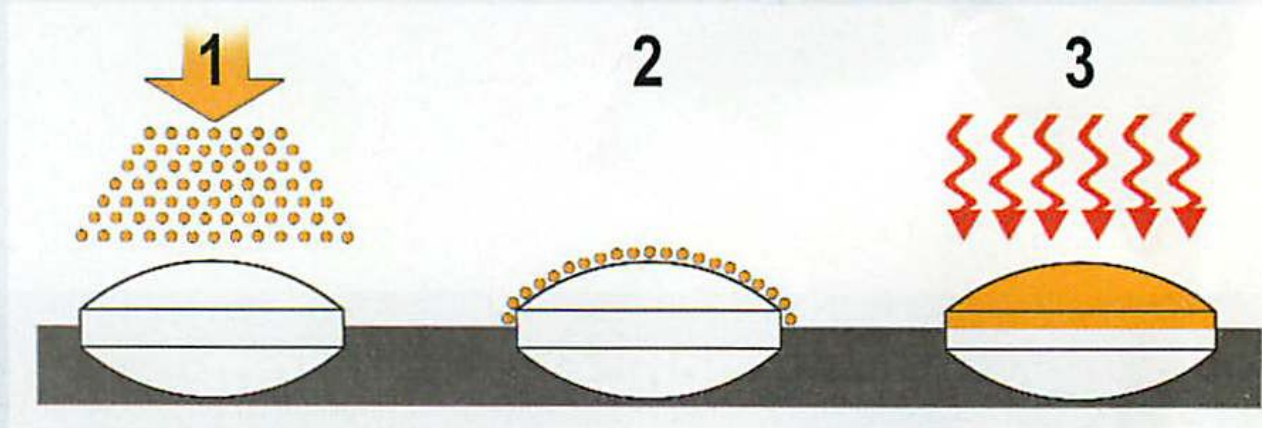
Delayed Burst Release

- Phoqus - 1



FIGURE 6

The Phoqus concept. Tablet rests on a band that carries it into a chamber, where a powder deposits upon it via electrostatics (1). The powder attaches only to the exposed surface (2). Infrared heat melts the powder into a film (3).



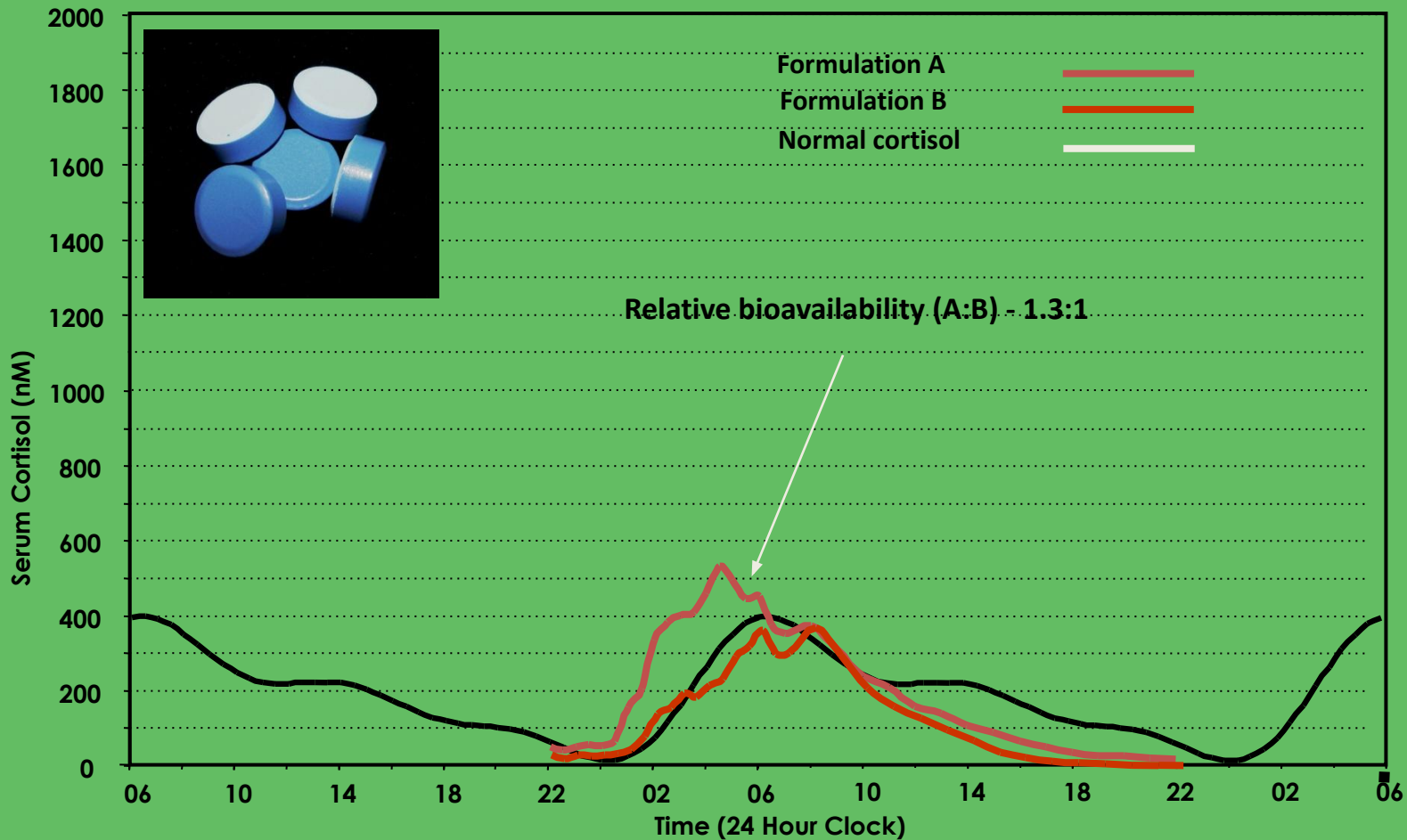
Original drawing by Edward Sharf

Erosion – II

Delayed Burst Release

- Phoqus 2





Newell-Price J, Whiteman M, Rostami-Hodjegan A, Darzy K, Shalet S, Tucker GT, Ross RJM. Modified-release hydrocortisone for circadian therapy: a proof-of-principle study in dexamethasone-suppressed normal volunteers. *Clinical Endocrinology* 68, 130–135 (2008).

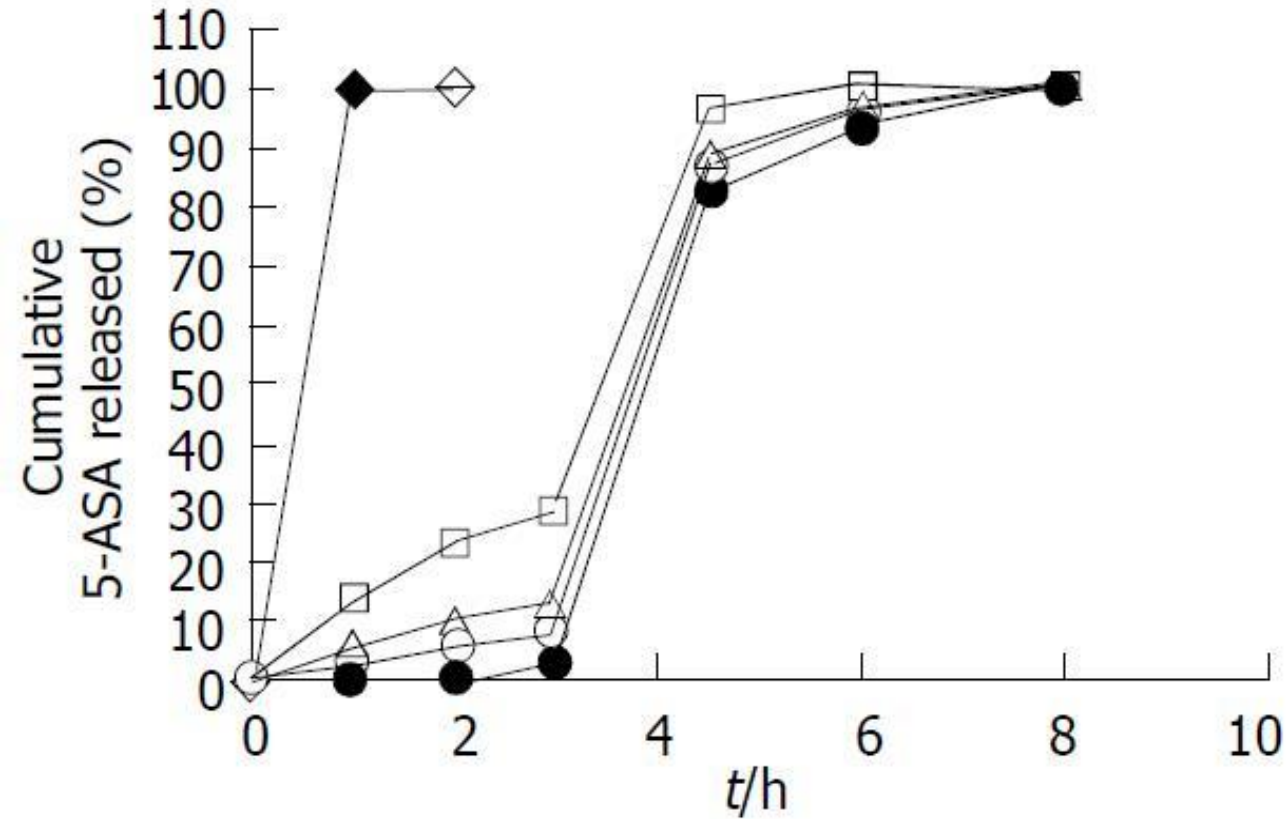
Photo Credit: Petr Pavlicek/IAEA
[https://commons.wikimedia.org/wiki/
File:4th_block_of_the_Chernobyl_Nuc
lear_Power_Plant.jpg](https://commons.wikimedia.org/wiki/File:4th_block_of_the_Chernobyl_Nuclear_Power_Plant.jpg)

Encapsulation



Eudragit L100 Delayed Release 1



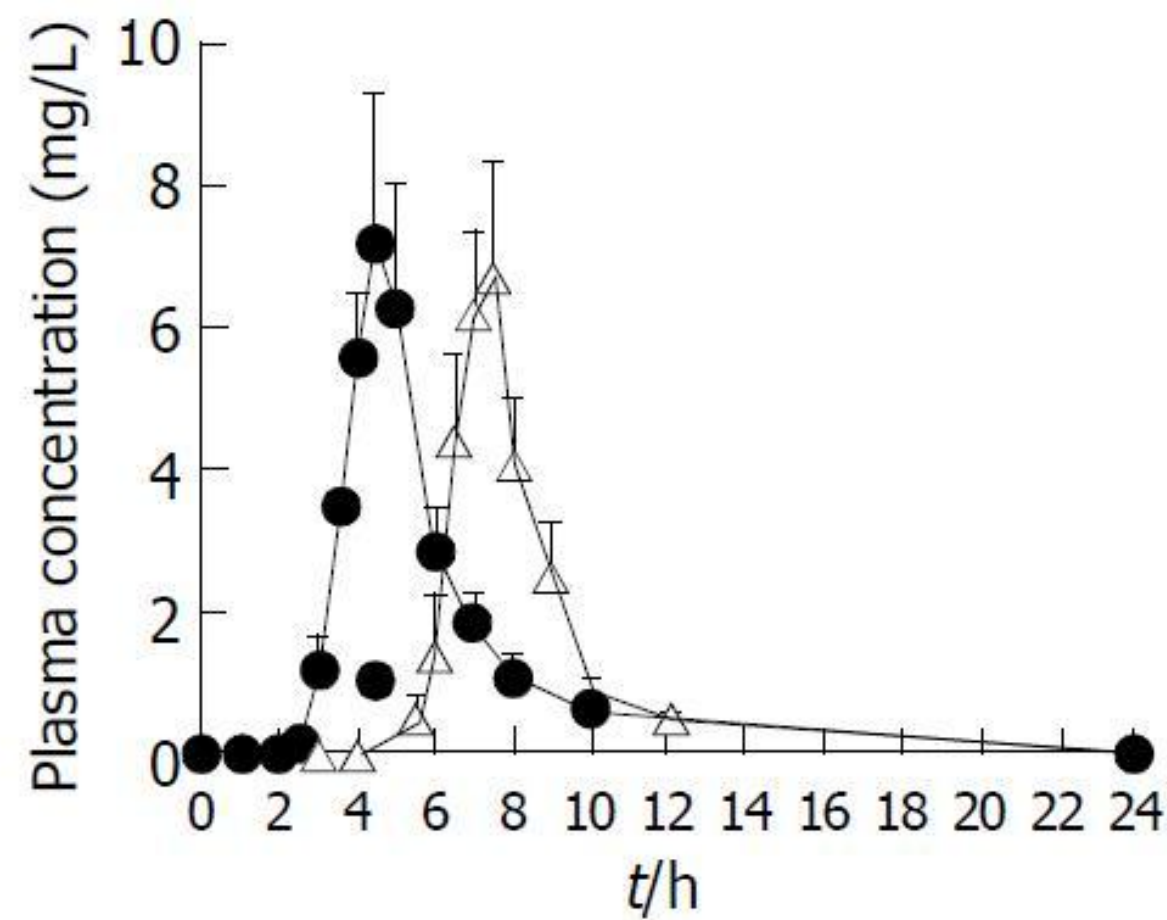


Cheng G, An F, Zou MJ, Sun J, Hao XH, He YX. Time- and pH-dependent colon-specific drug delivery for orally administered diclofenac sodium and 5-aminosalicylic acid. *World J Gastroenterol* 2004; 10(12): 1769-1774

Figure 5 5-ASA release profile of pellets coated at 5 levels of uncoated (◆), 5% (□), 10% (△), 15% (◐), 25% (●) (w/w, total solid applied) with Eudragit® L100-Eudragit® S100 combinations of 1:4 (w/w), using the sequential pH change method ($n = 6$).

Eudragit L100 Delayed Release 2





Cheng G, An F, Zou MJ, Sun J, Hao XH, He YX. Time- and pH-dependent colon-specific drug delivery for orally administered diclofenac sodium and 5-aminosalicylic acid. *World J Gastroenterol* 2004; 10(12): 1769-1774

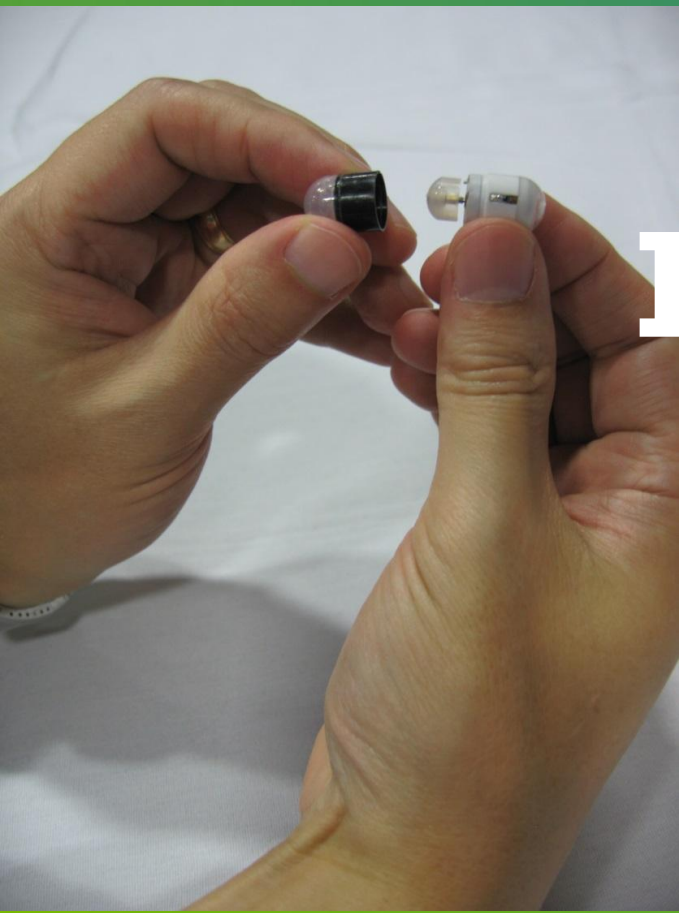
DS plasma concentration-time profiles after oral ad-ministration of coated formulation (△) and reference enteric formulation (●) in dogs at a dose of 100 mg/body.

Investigation of pH and Temperature Profiles in the GI Tract of Fasted Human Subjects Using the Intellicap® System

Mirko Koziolk, Michael Grimm, Dieter Becker, Ventzeslav Iordanov, Hans Zou, Jeff Shimizu, Christoph Wanke, Grzegorz Garbacz, Werner Weitschies

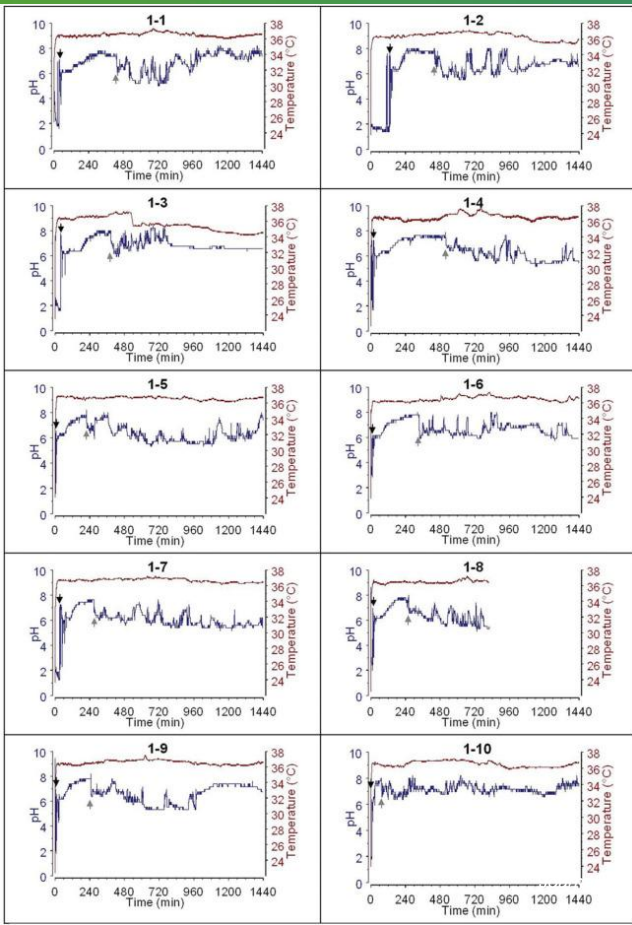
Journal of Pharmaceutical Sciences
Volume 104, Issue 9, Pages 2855-2863 (September 2015)
DOI: 10.1002/jps.24274





Intellicap

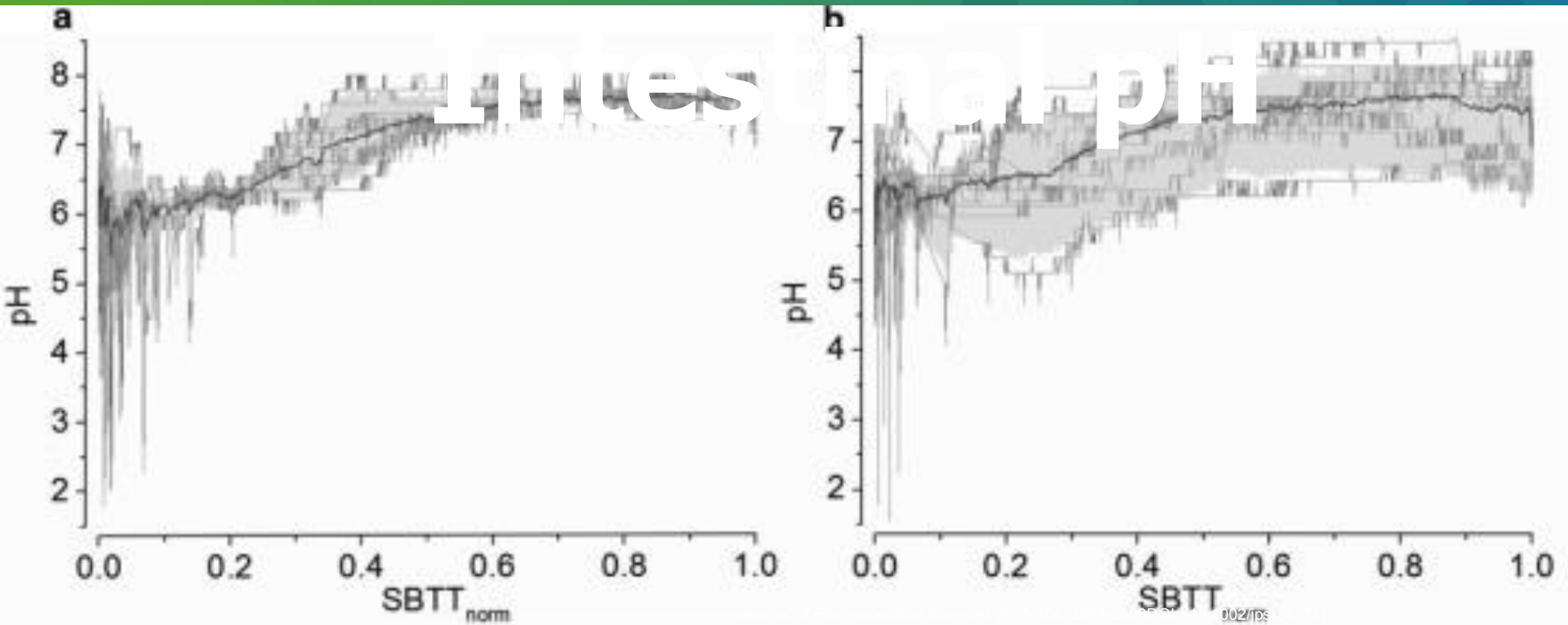




Temperature (red) and pH profiles (blue) during the first 24 h (1440 min) obtained after IntelliCap[®] ingestion in study 1. Gastric emptying is indicated by black downward arrow and colon arrival by gray upward arrow. In subject 1–8, the battery of data receiver was discharged after about 13 h.



Individual pH profiles (gray) of IntelliCap® in the small intestine over normalized small bowel transit time (SBTT_{norm}). (a) Study 1, (b) study 2; each study with $n=10$ subjects. The black line indicates the mean curve calculated by linear data interpolation. The shaded area represents the 10–90 percentile range.



PHARMACEUTICAL EXCIPIENTS

- An **Excipient** is usually an inert substance added to the drug to give suitable consistency or definite form to the drug. It is also called pharmaceutical necessity or aid.





Excipients are Inert,
right?

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Lessons learnt:

- Oral (controlled) drug delivery is INTERDISCIPLINARY
- Ignoring inconvenient “knowns” can be expensive/fatal
- Not trying to identify “unknowns” (to you) is stupid and potentially fatal
- The CRS exhibition is a great place to find resources: Suppliers, consultants, information and more
- The annual meeting is a great place to interact with people who might have your “missing link”
- Trust me: whether you are an individual or an organization, you cannot do it alone



Cheklis!-in random order

- Are you solving a REAL problem?
- Do know all the parameters? (NO, you don't!)
 - Do you understand the user? Physiology, ergonomics...
- Are you challenging the limits of (present) technologies (Theranos replay?)
- Is your budget realistic? (please, times 2 or 3...)
- Is your Intellectual Property protected? (do you need protection?)
- Did you ask around? (don't keep you cards TOO close to your chest)
- Accept that you need HELP!



Welcome to Reality!



Chris
<http://www.fireworks.com>

<http://www.fireworks.com>
hallelujah-sound
/Fireworks/Fire

**I hope you have (had)
a productive meeting
and workshop**

