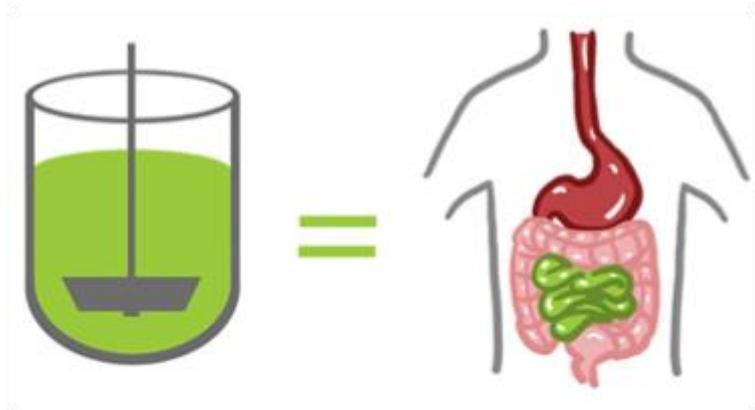


비교용출시험(*in vitro* comparative dissolution test)'을 통해서, 과연 약효동등성을 인정받을 수 있는가?



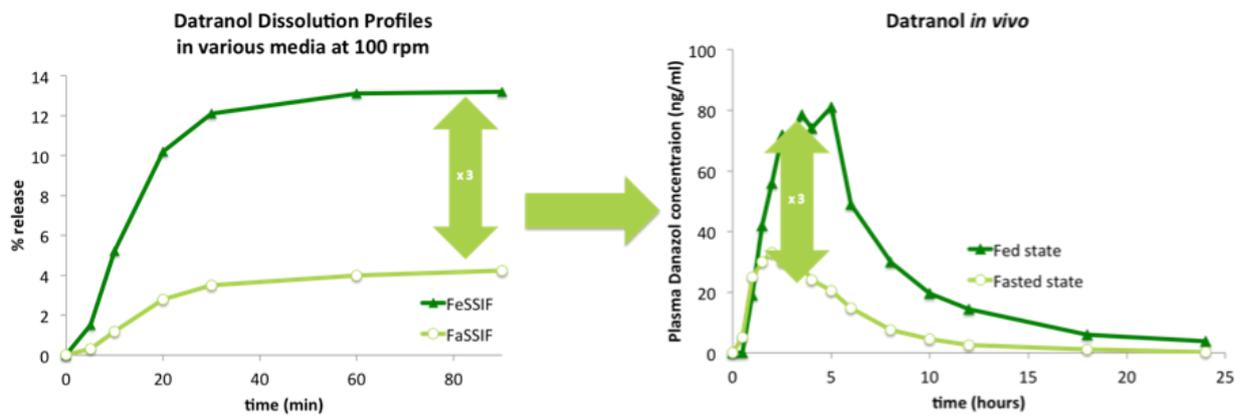
What's An 'In Vitro In Vivo Correlation' (IVIVC)?

[Drug Development](#), [Generic Drugs](#), [Industrial Use](#), [IVIVC](#), [PBPK](#)

During the development of oral drug formulations, it's important to find out if the right drug concentration arrives at the desired place of action.

Drug absorption is measured *in vivo*, in other words in a human (or animal) body. Typical *in vivo* indicators are 'time – blood plasma concentration profiles' of drugs after oral administration. To identify the parameters involved in drug absorption *in vitro* investigations are usually performed. *In vitro* literally means 'in glass' and depicts an investigation performed in an artificial environment mimicking a biological condition.

To establish a reliable *in vitro in vivo* relationship (IVIVC) it is important that the artificial environments simulate the biological conditions as closely as possible. On that basis the experimental results can directly be connected to real outcomes in humans. During drug development and formulation exploration, *in vitro* solubility and dissolution should artificially mimic the *in vivo* drug or formulation performance in the human gastrointestinal tract. The *in vitro* results are then related to *in vivo* drug plasma concentration profiles (see danazol example below). When an *in vitro in vivo* correlation is established, it is used for development and optimisation of drug formulations. Research organisations often use this method to reduce costly and time intensive trials on animals and humans during formulation development.



Nowadays computer models are often used to link *in vitro* results with *in vivo* outcomes. These so called physiologically based **pharmacokinetic (PBPK) models** are capable of translating *in vitro* results into *in vivo* predictions. This method is defined as *in vitro in silico in vivo* correlation (*IVISIVC*).

Establishing *in vitro in vivo* correlations for poorly soluble drugs (also referred as BCS Class II and IV) can be challenging. When it comes to investigation of drug dissolution performance in the simulated conditions of the gastrointestinal tract, simple buffers usually are not sufficient enough. In this case, [Biorelevant Media](#) should be utilized because they closely mimic the fluids of the human (and animal) stomach and intestine. Biorelevant Media have become the gold standard for *IVIVC* and *IVISIVC* investigations of poorly soluble drugs during formulation development.

비교용출시험(*in vitro* comparative dissolution test)'을 통해서, 과연 약효동등성을 인정받을 수 있는가?

경구용 약물의 체내흡수는 분해(*disintegration*)-용출(*dissolution*)-흡수(*absorption*)의 과정을 거친다. 이 중 용출의 양상을 시험관내에서 비교하는 것이 (비교)용출시험이고, 생체내 흡수가 이루어진 후 체내(혈중)농도 양상으로부터 두 제품을 비교하는 것이 생동성시험이다. 용출에서부터 흡수에 이르기까지의 과정에는 많은 생체요소가 관여한다.

만약 용출시험이 생동성시험과 대등한 수준의 자료로서 이용되려면, *in vitro-in vivo* 상관관계(*IVIVC*, *in vitro-in vivo* correlation)가 증명되어야 하는데, 좋은 *IVIVC* 라 함은 "in vitro 용출시험으로서 생체내 흡수 양상을 잘 예측할 수 있다"는 뜻이다. 이는 약물개발과정에서 요구되는 *in vivo* study 를 일부 *in vitro* study 로 대체할 수 있음으로 인하여 여러 측면에서 큰 이득을 가져오게 된다.

덧붙여 일반제형의 경우에는 일반적으로 *IVIVC* 가 없기 때문에, 일반제형에 대한 FDA

Guidance에서는 그 언급을 찾아볼 수 없다. 즉 일반제형에서 생동성시험을 일부 면제하여 주는 이유는 좋은 IVIVC를 입증하였기 때문이 아니고, 다만 위의 특수한 경우 흡수에 문제가 없을 것이라는 판단 때문이다.(만약 IVIVC 때문이라면, IVIVC를 확립하기 위해서 최소 한 개의 in vivo study가 요구될 것이다.)

서방제형의 경우, 아직 명확히 정의된 바는 없지만 통상 일반제형보다는 IVIVC를 보일 가능성이 높기 때문에, 용출시험이 제조과정상의 품질관리 목적 이외에도 in vivo 양상을 예측하는 데 쓰일 수 있다(Ref. 4,5). FDA Guidance에서는 IVIVC의 수준을 level A, B, C의 세 단계로 규정하고 있으며, 이 중 가장 좋은 상관관계를 보이는 level A의 경우에는 SUPAC(시판승인 후 제조과정 등 변경) 승인신청 등에 in vivo study를 일부 면제받을 수 있다. 그러나 IVIVC는 product-specific하기 때문에, 개별 품목별로 IVIVC를 확립하기 위하여 최소한 한 개의 in vivo study는 요구된다. IVIVC는 개발과정에서 전체 in vivo study의 개수를 줄여보고자 하는 데 그 의의가 있다.

실질 사용후기

My group has been using the media since before I joined. The products have been very easy to use and quick to arrive. It's been super easy ordering from you guys.

Pfizer Inc, USA

”



“

It is easy to use. The powder is not irritating when weighing. The containers (packaging) are very attractive. We are very satisfied with your product.

Lek Pharmaceuticals d.d., Slovenia

”



“

Biorelevant.com media have been a staple of our lab for the past year as we move into oral formulation development and testing. Your powders are easy to use, and the buffers are straightforward to make. I appreciate the ease with which we can make intestinal and gastric fluids for research purposes.

Princeton University, USA

”



“

I like the products very much. They are good for my analysis when simulating intestinal fluids.

Liconsal S.A., Spain

”



“

Meets expectations. Easy preparation. Fast delivery, simple instructions. The more compact bottle needs less space in the fridge. The webpage with calculations is appreciated.

Novartis Pharma AG, Switzerland

”



“

I think that the products offered are great for development work on dissolution method and the ease of use of the product provided made buying from your company a must for future method development. Service was extremely fast.

Lee Bertram, Gilead Sciences, Inc. , USA

”



“

Perfect for our dissolution work... the products are great with delivery always on time. Guys, keep up your good job!
Spectrum Pharmaceuticals Inc, USA

”

ZENTIVA

“

I think it's a good product for researching new medicines. Thanks for your work!
Lucie Krejčířová, Zentiva k.s., Czech Republic

”



“

We tested the 'FaSSiF/FaSSiF/FaSSGF' media for our research. The results were as desired. We will continue to buy the product.

Valentin Gallert, BioNTech Small Molecules GmbH, Germany

”



“

The range of powders from biorelevant.com is the fastest way to obtain reliable results for biorelevant solubility and dissolution testing.

Prof Jennifer Dressman, University of Frankfurt, Germany

”



“

We use it quite frequently and have never had issues with it. It is a great product.

Lilly, USA

”



“

Powders from biorelevant.com are really easy to prepare. They give reproducible results in our *in vitro* bioequivalence studies and we are highly satisfied with the products.

Fargem, Turkey

”

MAQUET

GETINGE GROUP

“

I got recommended it by my co-workers... I think it is really easy to use, especially since I'm not a Biochemist; I would not know where to start if I was going to make my own media.

Sofia Regnell Andersson, Maquet Critical Care AB, Sweden

”



“

It's great, much easier than making from scratch, saving time with no variability.

Fiona McInnes, Drug Delivery International (DDi), United Kingdom
”



**UNIVERSITÉ
DE GENÈVE**

“

It's a really good idea! The powder is the best way to have reproducible results. A big economy of time in the lab and money!

Fabrice Gillerat, University of Geneva, Switzerland
”



“

FaSSIF/FeSSIF/FaSSGF powder is very easy to use and gives consistent, reliable results. Instructions for use are very clear and correspondence from the company is swift and helpful. Great service too.

Tom Dennison, Aston University, United Kingdom
”



“

We use FaSSIF/FeSSIF/FaSSGF powder in our lab. The biggest benefit of using the powder is that it is very flexible and compatible with different buffers. We can then create Biorelevant Media at different pHs and buffer capacities. The powder is very easy to use. The biorelevant.com website provides a great resource in terms of preparing and using the media. The staff are very friendly and work efficiently!

Dr Fang Liu, University of Hertfordshire , United Kingdom

”



“

The powder from biorelevant.com is much easier to use, that's why we order it.

Acino Pharma, Switzerland

”



“

It is very easy to use. I am very pleased with the powder.

Galenica, Sweden

”



“

The powder is very easy to prepare, saves time and biorelevant.com provides excellent service.

Aurigene Discovery Technologies, India

”



“

Now there is only one way of preparation for us – FaSSIF/FeSSIF/FaSSGF, because there are only benefits. It saves a lot of time (by our calculations more than 50%) and the best part is very simple preparation. It's also very user friendly because with powder we can prepare low volumes of media (e.g. for solubility testing).

Krka, Slovenia

”

Hovione 

“

The powder from biorelevant.com provides a very practical and economical way to produce the FaSSIF medium.

Iris Duarte, Hovione Farmaciência SA, Portugal

”



“

We use powder from biorelevant.com for in vitro dissolution testing of the drugs in Biorelevant Media and it is very helpful to predict the in vivo behaviour of the drugs in this way. Preparation of the media is very easy and time saving with this powder.

Dr. Asuman AYBEY DOĞANAY, Ilko Ilac, Turkey

”

UNIVERSITY OF
COPENHAGEN



“

FaSSIF/FeSSIF/FaSSGF is very useful in the lab, especially during the development of a new method. Because it is so easy and relatively fast to make biorelevant media, you can focus more on the setup of a study.

Cecilie Madsen, University of Copenhagen, Denmark

”



“

The powder is very good, it is simple to use and stable.

Debiopharm Group, Switzerland

”



“

Service is the best, efficient and reliable. The powder from biorelevant.com is the ONLY material that we use.

Abbott Laboratories, Singapore

”



“

We use the powder for preparation of different biorelevant media (FaSSGF, FaSSIF and FeSSIF) for solubility and dissolution studies. The method of preparation of the media is very easy to follow and we get biorelevant media of high quality. The short time needed for their preparation and the reproducibility of the media are great advantages of this product. The support from the biorelevant.com team is excellent!

Dr Nikoletta Fotaki, University of Bath, United Kingdom

”



“

It is very easy to handle and take less time to prepare the solution.

Kazi Mohsin, King Saud University, Saudi Arabia

”



“

Quick to produce, saves time, consistent quality.
Nycomed, Germany

”

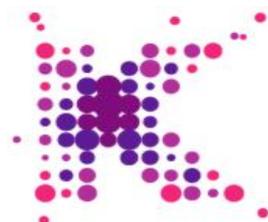


QUALITY CHEMICAL
LABORATORIES

“

We were impressed with the results...very easy to use and very easy to handle. This is our first purchase of the powder but I have no doubt we will continue to use it as our needs grow.
Johnny Brendell, Quality Chemical Laboratories, USA

”



kuecept
Drug Delivery Technologies

“

As a contract research and development company, obtaining solubility data in biorelevant media of our clients' drug molecules is essential in order to fully understand the challenges we are facing for oral drug development. This data also allows us to design our formulations intelligently based upon the physico-chemical properties observed. In order to design a robust formulation it is imperative that the preformulation data is also robust and the consistent quality of the powders from biorelevant.com allows us to obtain fantastic reproducibility; in addition, as they are so easy to prepare the time saving benefits can be passed on to our clients, both from a cost and time perspective.

Dr Mark Saunders, Kuecept Ltd, United Kingdom

”



National and Kapodistrian
UNIVERSITY OF ATHENS

“

The products are very helpful in regard to the amount of work needed for preparing the solutions. In addition, one does not have to worry for other potential issues, e.g. residual dichloromethane amounts in the rotavap.

Prof Christos Reppas, University of Athens, Greece

”



“

So far so good! Our order arrived promptly... the powder was easy to store, handle and transfer into the SGF media.

Collegium Pharmaceutical, USA

”

ratiopharm

“

We found the powder offered a very easy, convenient and reproducible way of preparing biorelevant media. For us it was an easy entry into this field and is now an ideal support during the preparation of bioequivalence studies.

Ratiopharm, Germany

”



“

I first heard about FaSSIF/FeSSIF/FaSSGF when I started working on drug dissolution studies at Nanocopoeia. I think the powder is an excellent tool in drug dissolution and absorption studies, and that it's extremely easy to use. From what I've seen in the literature, it seems as though its use in absorption studies is the industry standard.

Cole J. Batty, Nanocopoeia Inc., USA

”



“

It took only 10 minutes to prepare FaSSIF, this powder makes it easy to use biorelevant media.

Shionogi & Co. Ltd, Japan, Japan

”

“

FaSSIF/FeSSIF/FaSSGF is a very easy substance to use in our lab. It is easy to store and the website offers a great resource for actually making the media.

Metrics Inc, USA

”



“

We would consider the reproducibility of the measurements to be good. We routinely use the powders to make solubility and

dissolution measurements in FaSSIF and FeSSIF and find them easy to work with, efficient (in both economic and temporal terms) and reproducible.

Sirius Analytical, United Kingdom

”

Watson Pharmaceuticals 

“

I found the powder very easy to work with, and if there is no solubility issue with the drug, it works great and it's comparable to the conventional FaSSIF/FeSSIF media with egg lecithin which are too expensive and hard to work with.

Watson Laboratories, USA

”

U. PORTO

“

The powder is very useful and makes it easy to mimic the gastrointestinal system.

Ana Rute Neves, ICETA (University of Porto), Portugal

”

GOETHE 
UNIVERSITÄT
FRANKFURT AM MAIN

“

We routinely use powders from biorelevant.com in our transfer model to examine the supersaturation and precipitation behaviour of poorly soluble drugs. Not only is the media considerably quicker to prepare but its preparation is also significantly safer as dichloromethane is no longer required. We have been very happy

using the media so far and will continue to use the powders in the future.

Dr Edmund Kostewicz, University of Frankfurt, Germany

”

The Merck logo is displayed in a bold, blue, sans-serif font.

“

The powder is really good to show how API's and formulations work under biorelevant conditions. It is easy to use and handle. We test many API's with powder from biorelevant.com and have had good results.

Merck KGaA , Germany

”



“

I really like it. The powder has been great!

Ross Barman, MIT, USA

”



“

Great product, easy to use thanks to the interactive website/tables.

Max Finch, Emerson Resources Inc, USA

”



“

El producto es genial, las instrucciones son de fácil entendimiento y muchas aplicaciones con un solo envase. La página de Internet tiene muchas funciones interesantes.

The product is great, the instructions are easy to understand and there are many applications for a single container. The website has many interesting uses.

Angioletta Coto Quesada, Stein Corp, Costa Rica

”



UNIVERSITY OF MINNESOTA

“

The products are very helpful for my project... everything is great!
University of Minnesota (Science and Engineering), USA

”



“

I think these products are great. We have some simulated solutions we make but this is great for adding some components that we don't normally use. I also like that the same product can be used for fed and fasted intestinal conditions with different prep.

Dow, USA

”



“

These products are great!
Absorption Systems , USA

”

biorelevant.com >> All Types of Biorelevant Media