GI Foresight™

Optimising oral administration

Biopta Ltd is a Contract Research Organisation specialising in GLP testing in ethically-obtained human tissues. We believe *in vitro* testing in human tissue, the closest model to human *in vivo* function, provides invaluable data to accurately identify compounds with the greatest likelihood of clinical success, reducing the risk of late stage failures and streamlining preclinical development.

Due to its convenience and safety profile, the oral route of administration is one of the preferred methods of drug delivery. This means that the interaction of a drug with the gastrointestinal tract is an important factor in its pharmacokinetics, safety, bioavailability and, ultimately, efficacy. Routinely, assessments of these factors are carried out using *in vivo* or cell assay models; however at Biopta we are able to provide powerful supporting data in functional human tissues, entirely in compliance with GLP.

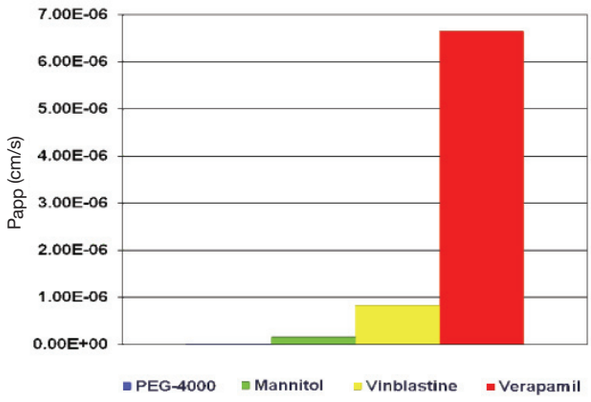
Profiling in human tissue delivers accurate data on your compound in man, reducing the extent of *in vivo* animal testing required and eliminating species variation. It is Biopta's recommendation that human *in vitro* pharmacology testing is carried out as part of your preclinical development program, delivering powerful human safety data prior to expensive Phase I/IIa studies.

GI Foresight™

GI Foresight™ is a package specially designed to optimise the development of drugs for oral administration. Absorption of each compound is assessed and effects on motility are established. Absorption data provide vital information on efficacy, while alterations in gut motility can have safety implications and can indirectly influence the rate of absorption. Tissue from the same patient can be used for both permeability and gut motility studies.

Permeability studies

Absorption across gastrointestinal mucosa is tested in the Ussing chamber. Compounds can be ranked in order of permeability, compared to our in-house standards and active efflux processes can be highlighted. Any part of the GI tract can be investigated and both hot and cold assay options are available.



Compound	Human P_{app} cm/s	Clinical Fraction absorbed
PEG-4000	6.43E-09	0-2%
Mannitol	1.57E-07	15-17%
Vinblastine	8.21E-07	NA
Verapamil	6.66E-06	95-100%

Figure 1: *Papp of standard compounds compared with clinical values for fraction absorbed.*

Standard compounds ranked according to their apparent permeability (P_{app}) in human duodenum are comparable to clinical values for fraction absorbed (F_a). Mannitol and PEG-4000 are non-permeable markers, vinblastine is a moderately permeable substance which is subject to active efflux and verapamil is a highly permeable substance.

Continued on reverse.

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GI Foresight™
Optimising oral administration continued

Effects on gut motility

Gut motility effects are assessed in organ bath experiments using muscle strips, which can be taken from any part of the GI tract. Strips can be stimulated with electrical impulses or drugs and the effect of compounds on these responses assessed.

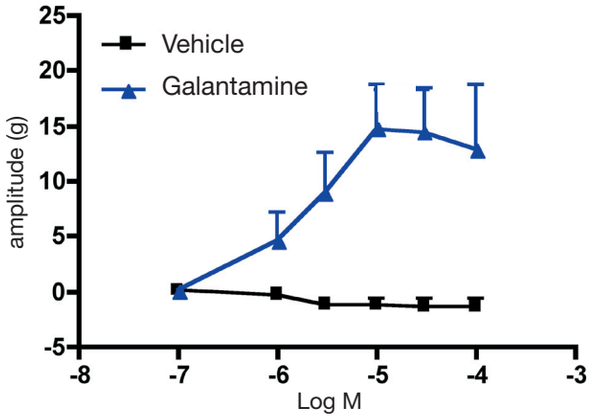

Figure 2: *Effects of galantamine on EFS amplitude in human stomach.*

Why use Human Tissue Rather than Animal Models or Cell Line Assays?

Many animal models and cell lines represent entirely adequate test systems for specific purposes; however, differences in the typical responses do exist and create uncertainty about the predicted profile in humans. The use of fresh human tissue avoids unforeseen species differences, which can lead to misinterpretation of permeability and safety data, not only for drugs that later prove to be unsuitable, but also for drugs that may be wrongly classified as unsuitable based on responses in animal or cell line assays.

Benefits of Human Tissue Testing

- Strengthens IND submissions
- Avoids species differences
- Adds commercial value by generating human data during preclinical development
- Improves decision-making processes based on functional human data
- Reduces the risk of late stage failures

References

1. Wilkinson (1971). Gut; 12; 654 – 660

2. Grés et al. (1998) Pharmaceutical Research; 15 (5); 726 – 732

3. Li et al. (2008) Drug absorption studies, Springer US. Chapter 18

4. Balimane et al. (2006) The AAPS Journal; 8 (1); E1 – E13

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