



Absorption and Efficacy

In vitro studies

Our **dedicated labs** develop customized ***in vitro* models** for different applications.

Absorption and efficacy *in vitro* studies

In vitro models mimicking different biological barriers can be adopted to perform absorption studies and evaluate efficacy of products, ingredients or new formulations before to proceed with the next step evaluation (e.g. clinical trial).

In vitro methods are less expensive, faster, and offer better controls of experimental variables than human or animal studies, so they can be easily exploited as **screening, ranking, or categorizing tool**.

Why choosing *in vitro* models?

Reasons for *in vitro* studies to be the better option are the following:

1. reduce costs and time
2. more directly assess product performance as:
 - select the best endpoints to be investigated by clinical studies
 - definition of posology
 - select the most promising prototype / formulation

What kind of studies?

Investigation of mode of action of active substances to support patent and scientific publications/marketing.

Bioaccessibility

Fraction of active substance released by the product during gastrointestinal digestion and available for absorption.

Bioavailability

Fraction of active substance absorbed by the body and able to reach the blood circulation.

Efficacy

Ability of an active substance to perform its function on a biological tissue.

Safety

Formulations and/or active ingredients must not have adverse effects on biological tissue.

The 3R

- Reduce time
- Reduce cost
- Reduce the % of clinical trial failure

3R

In which fields?

- Pharmaceuticals
- Dietary & Food supplements
- Novel foods
- Fortified foods
- Medical devices
- Cosmetics

Our capabilities

Mérieux NutriSciences can support all your projects with a wide range of *in vitro* models.

Screening protocol study

Dissolution test

- **STANDARD DISSOLUTION TEST according to EP/USP**
Bioaccessibility assessment with simulating liquids (pH).
- **DELAYED/GRADUAL RELEASE DISSOLUTION TEST according to EP/USP**
Bioaccessibility assessment with simulating liquids (pH) and delayed/gradual release check.

Absorption test shot-gun analysis

PRELIMINARY BIOAVAILABILITY ASSESSMENT - systemic level (for internal use information)

Gastro-intestinal absorption study using a 2-step *in vitro* model:

- **STEP 1.** Gastro-intestinal exposure.
- **STEP 2.** Preliminary bioavailability assessment - systemic level (for internal use information).
Single step intestinal absorption study: advanced intestinal epithelium *in vitro* model (Caco2).

Complete protocol study

Absorption test complete study

BIOAVAILABILITY ASSESSMENT - systemic level (regulatory and/or scientific-disseminating use)

Gastro-intestinal absorption study using a 2-step *in vitro* model:

- **STEP 1.** Bioaccessibility / gastric digestion phase resistance assessment through oral-gastro-intestinal digestive process *in vitro* model.
- **STEP 2.** Intestinal absorption assessment through advanced intestinal epithelium (Caco2).

Absorption test complete study with advanced customized model

BIOAVAILABILITY ASSESSMENT - systemic level (for regulatory and/or scientific-disseminating use)

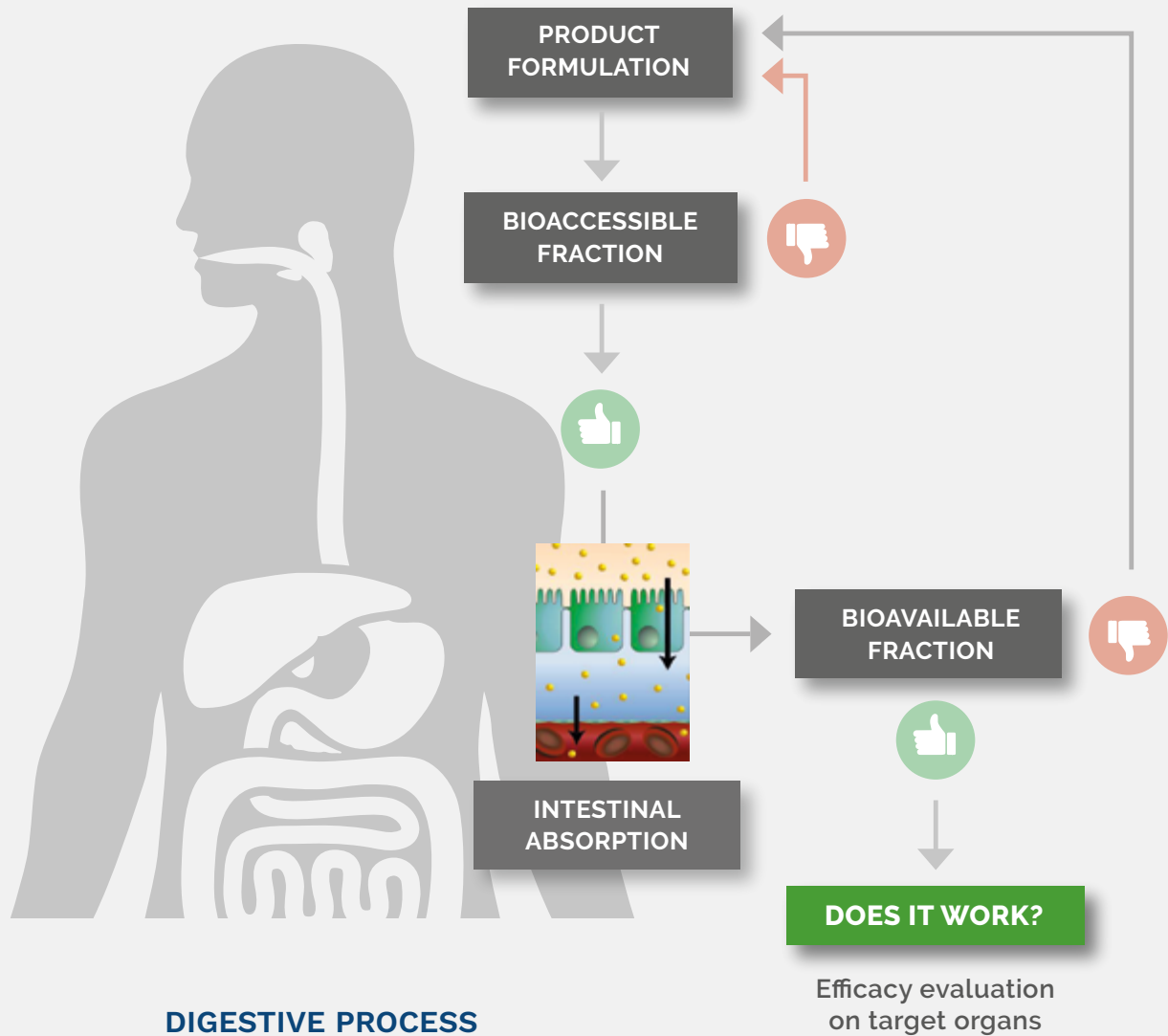
Gastro-intestinal absorption study using a 2-step *in vitro* model:

- **STEP 1.** Bioaccessibility / gastric digestion phase resistance assessment through oral-gastro-intestinal digestive process *in vitro* model.
- **STEP 2.** Absorption on customized advanced intestinal epithelium (Caco2) and/or pathological situation simulation.

Our *in vitro* models available

- Oral-sublingual models
 - Gastro-intestinal models
 - Mucosal models
 - Hepatic model
 - Prostate model
 - Cardiovascular model
- and other ad hoc model can be developed*

Formulation efficacy evaluation



Our dedicated labs can develop various and customized *in vitro* models for different applications able to **mimic the effects of drugs through biological models and absorption studies**, performing several screening tests to preliminarily evaluate product, ingredient or formulation before to proceed with the next step evaluation.

The **biological models** are composed of biological fluids that can represent digestive process, plasma serum, brain tissue, heart and blood, prostate and many others. All the models are **implementable and adaptable** according to the type of fluid or study to be carried out, and according to the customer's needs.

Efficacy studies with *in vitro* models

TEST	MODEL	DESCRIPTION
ABSORPTION EVALUATION		
Barrier action <i>Permeability reduction</i>	EPITHELIUM	Ability to limit substances access: preliminary cytotoxicity test - absorption study (1 timepoint) - instrumental analysis - comparative study on treated and not treated sample.
Barrier action <i>Anti-adhesive activity - microorganisms adhesion (CFU)</i>	EPITHELIUM	Ability to limit microorganism adhesion: preliminary cytotoxicity test - microorganism count - comparative study on treated and not treated sample.
Protective effect	EPITHELIUM	Ability of a product to eliminate or to mitigate the adverse effect of a harmful substance on a biological tissue: Cell vitality (i.e. MTS) - Cytotoxicity (i.e. LDH assay) - Apparent permeability (i.e. LuciferYellow) - Trans-epithelial electrical resistance (TEER) - Inflammation (i.e. IL-1 α release).
Adsorption efficacy evaluation	FRANZ CELLS	Compare the oral/intestinal penetration of different molecules or different formulations.
EFFICACY EVALUATION		
Regenerating action	EPITHELIUM	The regeneration efficacy will focus on 2 parameters: cell proliferation, and ATP production.
Soothing action	EPITHELIUM	The lenitive efficacy will be determined as decrease of IL-6 and IL-8 release with respect to the positive control.
Antioxidant activity - basic	EPITHELIUM	Activity of cellular free radicals scavenging systems: Glutathione system (GSH/GSSG) oxidation state of the glutathione pool - Superoxide dismutase (SOD) enzyme, activity and expression - Glutathione Transferase determination.
Antioxidant activity - extended	EPITHELIUM	Activity of cellular free radicals scavenging systems: Glutathione system (GSH/GSSG) oxidation state of the glutathione pool - Superoxide dismutase (SOD) enzyme, activity and expression - Glutathione Transferase determination - Inhibition of free radical (ROS) formation (i.e. DCFDA assay) - Lipid Peroxidation.
Chelating and detoxifying activity	DIGESTIVE PROCESS	ICP-MS analysis of heavy metals in different fractions and functional value of the digestive fluids.
Mucoadesivity test	ORAL MUCOSA or INTESTINAL EPITHELIUM	The test permits to evaluate the ability of a substance to bind to mucous membrane cells. Specific assay on treated and not treated sample.

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