DOCTORS' ANALYTICAL LABORATORIES PVT. LTD.
Testing for a better world

IN-VITRO BIOEQUIVALENCE

How do you prove a drug works the same when the body never absorbs it?

Sucroferric Oxyhydroxide 500 mg chewable tablets · Phosphate binder

A study-design walkthrough

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THE PROBLEM

No absorption means no blood levels to compare

1 A binder, not a systemic drug

The active, polynuclear iron(III)-oxyhydroxide, is practically insoluble. It works inside the gut and leaves the body unabsorbed.

2 Classic PK studies don't apply

With nothing reaching the bloodstream, a standard pharmacokinetic BE study can't show sameness.

→ So the test moves to the lab

USFDA's product-specific guidance asks generics to show equivalence through **in-vitro phosphate binding studies**.

Reference product: Velphoro® (US approval 2013)

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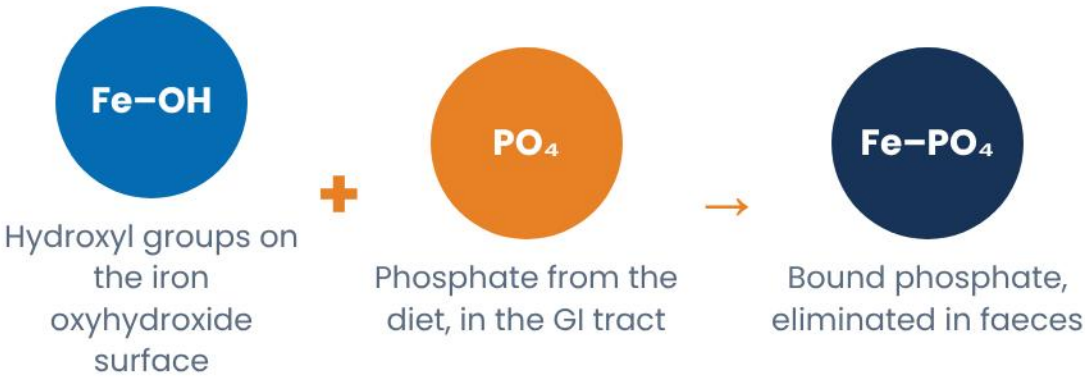
HOW IT WORKS

It traps dietary phosphate by ligand exchange



Binding has to hold across the gut's whole pH range, which is why the in-vitro study tests at two very different conditions:

pH 3.0
Stomach-like, acidic

pH 7.5
Intestine-like, near neutral

Mechanism per US prescribing information

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WHAT USFDA ASKS FOR

Two binding studies, run under tight control

E **Equilibrium**

At least 8 phosphate concentrations, binding measured at equilibrium

K **Kinetic**

At least 8 time points up to 24 hours, showing how fast it binds

- **Whole tablets** incubated, at pH 3.0 and pH 7.5
- **37 °C** with constant gentle shaking
- **pH checked every 15 minutes** and adjusted until equilibrium holds
- **12 replicates** of every binding study

Source: USFDA draft product-specific guidance

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THE SCALE OF IT

One "simple" binding claim. Thousands of data points.

8

pivotal studies: 2 equilibrium + 6 kinetic (low, mid, high at each pH)

96

sets: every study repeated 12 times

3,840

samples in the pivotal phase alone

~7,000

injections across validation (~2,500) and pivotal (~4,500)

16

parameters per method validation, to ICH Q2 and USFDA

~3,650

test and reference tablets, end to end

Planned study design

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FROM THE BENCH

Two tablets of the same drug don't behave the same in a flask

1 Dispersion

One product dispersed in 2–3 minutes; the other needed 6–8 minutes with sonication.

2 pH drift

Starting pH and the acid needed to hold it differed widely, before and after phosphate spiking.

3 Phase separation

Settling times ranged from 5 to 15 minutes, which changes when you can sample.

✓ So we optimised every variable

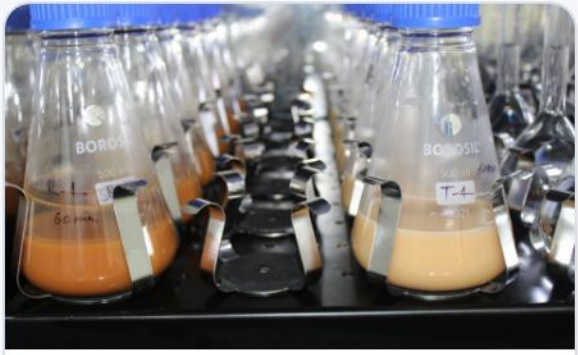
Sonication time, shaker RPM and pH control, with ~100% recovery confirmed in aqueous and placebo controls.

INSIDE THE LAB

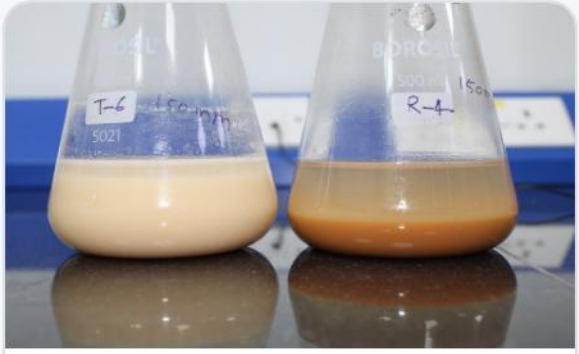
The study, up close

1 Whole tablets dispersing

2 pH adjustment, before phosphate



3 Final samples on the shaker



4 Phase separation, test vs reference

DALPL in-vitro lab, Navi Mumbai

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TIMELINE

From first experiment to submission-ready data

2 MONTHS — **Method development**
Two methods, one per binding study

2 MONTHS — **Method validation**
Two validations, at pH 3.0 and pH 7.5

1 MONTH — **Pilot studies** (optional)
Eight studies to de-risk the pivotal run

3 MONTHS — **Pivotal studies**
Eight studies × 12 replicates, test vs reference

Total, end to end **~8 months**

Indicative, per study plan

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Planning an in-vitro BE package for a non-absorbed drug?

Our pharma division in Navi Mumbai does:

- In-Vitro Binding Studies
- NG/G Tube Studies
- IVRT / IVPT
- Method Development & Validation
- Multipoint Dissolution

US FDA Inspected

Health Canada Approved

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Let's talk study design →