

Liver La Vida Loca!



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How the **Liver** turns drugs **Upside, Inside,** and '**Round** before they're **Out** of you

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Whether you're a Latin superstar taking a post-show aspirin for your aching hips, or sleepless and sipping on your daily coffee fix, chances are you've probably encountered drugs in some shape or form.

Drugs are everywhere! And with average life expectancy on the rise,¹ chances are you'll probably add a prescription medication or two to your cabinet in your lifetime.

This all begs the question:

How much do you really know about drugs?

In this article, we'll explore how our bodies process these ubiquitous substances as we delve into the science of *drug metabolism*. As you'll learn, drug metabolism involves a sensual dance between the liver and other organs. We'll also take a look at the one-two step of metabolism: Phase 1 & 2 reactions.

What is Drug Metabolism?

It refers to the chemical transformation of pharmaceutical drugs, such as aspirin, into forms that can be removed more easily from the body.² The product of these reactions are called metabolites.

To the body, drugs are foreign substances, so metabolism is its way of disposing them.³ This process involves the help of enzymes, the body's accelerator pedal.

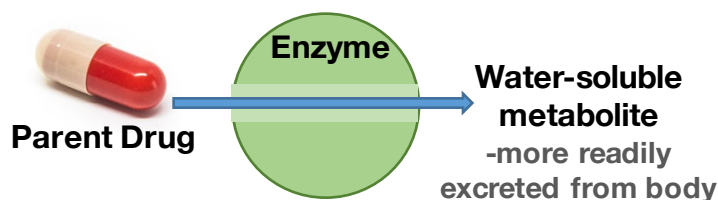
Enzymes speed up the rate at which drugs are altered into a more water-soluble form, which allows them to be dissolve more easily in the blood and be excreted via the urine and/or bile.⁴

The Liver's Star Role in the Dance of Drug Metabolism

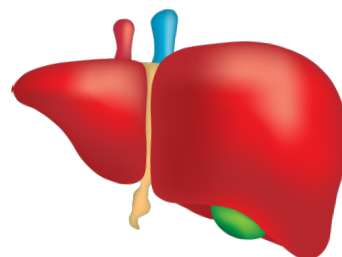
While drug metabolizing enzymes are found throughout the body, they're concentrated most in the liver.⁵ Here, drugs undergo two broad types of chemical reactions:

Phase 1 and 2 reactions.

While some drugs may undergo just phase 1 or phase 2, most undergo phase 1 followed by phase 2 in tandem.^{2,5} It's why these phases can be thought of as the one-two step of drug metabolism.



Drug metabolism involves the enzymatic conversion of a drug into a water-soluble metabolite.



If we're to think of the body as a dancefloor, the liver delivers the star performance, accounting for the vast majority of metabolic activity!

SCIENCE daily

The One-Two Step of Drug Metabolism

Phase 1 and 2 metabolism refer to a range of chemical reactions. They can be distinguished by a number of unique features, as shown in the table below.

	Phase 1	Phase 2
Type of reactions involved	Addition or exposure of a small functional group, such as: -OH, -NH ₂ , and -SH. ⁶	Attachment or 'conjugation' with large, water-soluble molecules, such as sulphates or amino acids. ⁷
	Oxidation (most common) Hydrolysis Reduction ⁸	Conjugations
Main enzymes involved	Cytochrome P450s ⁶	Transferases ⁷
Change in water solubility of product	Slight increase	Large increase
Pharmacological activity of product	Can be less or more compared to parent drug	Usually completely inactive

KEY FACTS:

- Most drugs undergo phase 1 followed by phase 2, such as aspirin.
- Phase 1 typically prepares a drug for conjugation in phase 2. Conjugation in turn dramatically increases the water solubility of metabolites, allowing them to be readily excreted.
- Notably, in phase 1 the metabolite can become more reactive or toxic than the parent drug with the addition of a functional group. This is an important factor to consider when prescribing or designing drugs!

Noteworthy Phase 1 Metabolites

Enalapril is used for the treatment of high blood pressure and chronic heart failure. However, the compound itself has no pharmacological activity; its metabolites do.⁵

Codeine is used for pain relief. Like enalapril, it exerts its effect on the body once it's been converted to *morphine* via phase 1 metabolism.⁹

The dance of drug metabolism is one we're all well versed in, whether we realise it or not. However, next time you sip your coffee or pop an aspirin, you can now be a little more thankful of the body's star performer as undergoes the *liver la vida loca*.

You don't phase me!



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