A PLAIN-LANGUAGE GUIDE TO HOW DRUGS WORK

The Straight Facts Guide to Drugs

No judgement. No scare stories. Just the numbers, the timing, the mechanics — and how to look them up for yourself.

Written from lived experience · For education, not encouragement

Contents

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How to Use This Guide

This guide exists for one reason: to explain what actually happens when a drug enters your body — the math, the timing, the mechanics, and the variables — so that whatever you decide, you decide based on the knowledge you've acquired.

It was written from lived experience, for three kinds of readers: people who use, people who teach or support others, and people who simply want to understand. There is no moralising in these pages and there are no horror stories. Fear is a terrible teacher; pharmacology — the science of how drugs move through the body — is a much better one. Every principle here applies whether a substance is prescribed, legal, or neither.

> **THE ONE RULE**
> If you don’t know the numbers, you’re gambling. Every section of this guide exists to replace guessing with knowing.

What this guide is **not**: it doesn’t tell you whether to take anything, and it doesn’t give doses for specific substances — those numbers differ per drug, per route, and per person. Section 5 shows you exactly where to find reliable ones. What you’ll learn here is the framework that lets you read those numbers like a professional.

> *A note on scope: this is an educational resource, not medical advice, and nothing in it should be read as encouragement to use any substance. Laws vary by country; pharmacology doesn’t. If you’re worried about your own use or someone else’s, a doctor or local harm-reduction service is a good, judgement-free place to start.*

Introduction — Knowledge is Power

The safest way to avoid harm through illicit drug use is not to use them. Saying that, if you are going to use them then teaching yourself the basic facts about how drugs work is probably the next best thing. The simple truth is some drugs have wider margins and mistakes aren't deadly. Others have very narrow margins and mistakes are deadly. Understanding why, and how to dose and take your preferred drug of choice can save yours and others lives.

Who am I?

Of course, I'm not going to tell you who I am in any detail that will reveal my true identity, much like a superhero I need to keep my real world identity secret.

The most I'll say is that I was born in the 1970s and experienced the early days of rave culture in the 80s and 90s. I was ordering off the dark net on the original silk road way before Joe Rogan “discovered” DMT, and Bitcoin was less than $30. If only I'd kept my Bitcoin instead of buying drugs, eh? I've used all the common ones, uncommon ones and research chemicals. I've never injected, and that is the advice I give to everyone, nor have I used Opioids outside of pain meds after operations. I still dabble from time-to-time, and I still use the same approach and logic that I present here.

I'm scientifically literate across many domains, everything written here is basic high school science. It isn't difficult to understand and I hope that I've presented it in an easy way to understand. I've taught my children this advice as well as handed it out to anyone that asks. I see lots of well meaning advice given on forums which just isn't factually true. So I decided to put it all down in one simple guide.

At the end of this guide you'll find my crypto information. If you feel inclined to give an old raver a tip then you can. But no worries if you just read this information and learn from it. The least I'll ask is that you share this guide with others who may benefit.

What's your name?

What have you had?

Reach for the lasers.

Safe as fuck.

Jeremy Faxman.

Section 1: The Foundation — The Math of Your High

Every drug has a predictable mathematical relationship with your body. This section is about the line between a good night and a medical emergency — and why that line is drawn by a curve, not a straight line.

1.1 The Dose-Response Curve (The "S-Curve")

MYTH — "If 100 mg feels good, 200 mg will feel twice as good."

FACT — Drugs don't work on a straight line — they work on a curve shaped like an "S". Doubling the dose never doubles the fun, and past a certain point it adds no fun at all.

The curve has four zones, and you are always somewhere on it:

- **The flat start.** At low doses, nothing happens until you hit the **threshold** — the first dose that produces any noticeable effect at all.
- **The sweet spot.** Just past the threshold, a small increase in dose causes a big jump in desired effects. This is where the target experience lives.
- **The plateau.** Eventually your brain's receptors are 100% occupied. Taking more drug will not make you higher — there is literally nowhere left for it to land.
- **The toxic cliff.** While the pleasure curve plateaus, the side-effect curve keeps climbing steeply. The excess spills over into heart strain, overheating, or organ damage.

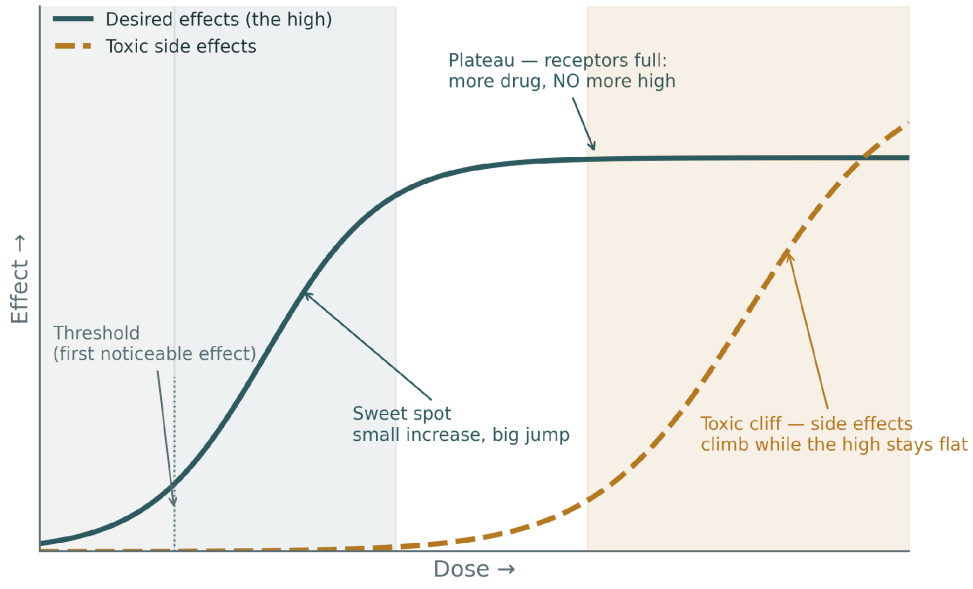

Figure 1 — The dose-response curve: desired effects plateau while toxic effects keep climbing (conceptual illustration).

1.2 The Four Critical Pillars of Any Dose

Before any substance enters your body, there are four numbers worth knowing, all measured in milligrams (mg):

- **Threshold dose** — the bare minimum needed to feel any effect at all.
- **Light / common dose** — the standard range where desired effects happen with manageable side effects.
- **Heavy dose** — the zone where side effects begin to outweigh the positive effects.
- **Lethal dose (LD50)** — the statistically calculated amount that causes death.

1.3 How the Numbers Are Calculated

These numbers aren't arbitrary. They come from a mix of clinical animal models, human trials, and decades of emergency-room data — and knowing where they come from tells you how much to trust them.

Threshold dose

How it's calculated: researchers use the Up-and-Down Method in human trials. Subjects are given microscopic, unnoticeable amounts of a compound, and the dose is raised in tiny steps across test groups until the very first measurable change — altered heart rate, pupil dilation, a reported psychological shift — appears reliably.

> *The Guide's Note: this is the absolute baseline. Anything below it is a sub-threshold or "micro" dose.*

Light / common dose

How it's calculated: this is built around the **ED50 (median effective dose)** — the exact dose at which 50% of trial subjects experience the desired effect. Researchers look for the point on the S-curve where positive effects peak while side effects stay low and manageable.

> *The Guide's Note: for illegal or novel substances there are no trials, so harm-reduction groups standardise this by aggregating thousands of self-reported user data points alongside hospital toxicology reports.*

Heavy dose

How it's calculated: this tracks the **TD50 (median toxic dose)** — the dose at which 50% of subjects experience specific, severe side effects such as extreme vasoconstriction, panic, or tremors.

> *The Guide's Note: in recreational terms, "heavy" means you've crossed the peak of the S-curve. Receptors are saturated, so the extra amount only amplifies toxic side effects without increasing the high.*

Lethal dose (LD50)

How it's calculated: LD50 means **Lethal Dose, 50%** — the dose required to kill 50% of a tested population. Because human testing is unethical, scientists test standard animal groups and translate the results using **allometric scaling**, a formula that adjusts for human body surface area and metabolic rate.

> *The Guide's Note: for illicit drugs, the human LD50 is further refined by forensic pathologists analysing blood-chemical concentrations in fatal overdose cases. It's a statistical boundary, not a target to flirt with.*

1.4 The Therapeutic Index (The Safety Margin)

The **therapeutic index** is the mathematical gap between an effective dose and a dangerous one. That gap — not the substance's reputation — is what determines how forgiving a drug is of mistakes.

- **Wide margin (e.g. cannabis, psilocybin):** the distance between an effective dose and a dangerous dose is massive. Getting the dose wrong by eye is unlikely to be physically dangerous.
- **Narrow margin (e.g. heroin, GHB, 4-MMC):** the distance is razor-thin. Eyeballing a dose, or adding a tiny fraction of a gram, can push you from a "common dose" straight into a lethal one. These are the substances where a milligram scale is not optional.

Two drugs can feel equally intense while having completely different margins. Intensity is what you feel; the index is what can hurt you. Same S-curve shape, wildly different geometry:

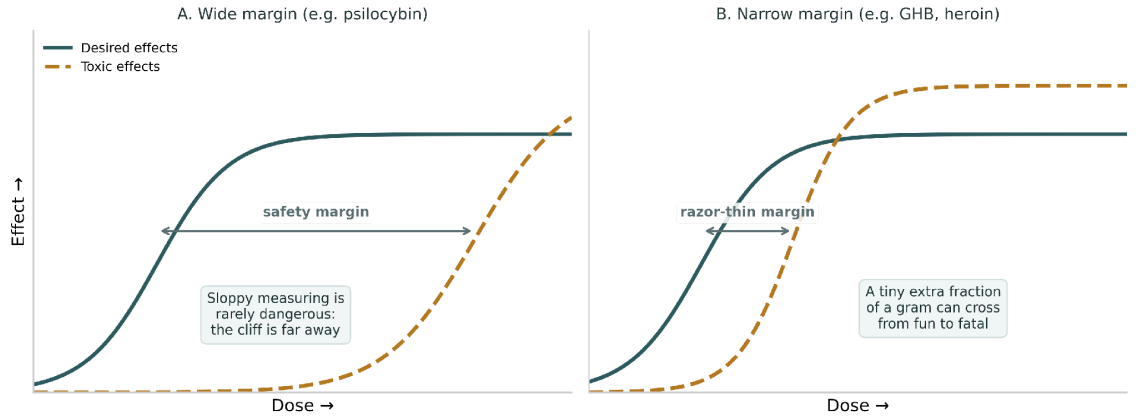

Figure 2 — Every drug has its own S-curve: the gap between the desired-effects curve and the toxic-effects curve is the therapeutic index (conceptual illustration).

1.5 Myths vs Pharmacological Facts

MYTH — "Just take a little bit more if you don't feel it after 20 minutes."

FACT — This ignores the drug's onset timeline entirely. You're stacking a second dose on top of a first one that hasn't even arrived yet — shifting your position on the curve straight into the toxicity zone. Section 2 shows the math.

MYTH — "Pure gear means you can take more, safely."

FACT — Pure gear means you need less. High purity shifts the dose-response curve backwards, so a standard street-weight dose of a purer batch can actually be a massive overdose.

MYTH — "I've had this exact dose before, so I know how it goes."

FACT — The dose is only one of four variables. Your tolerance, your body, your route, and whatever else is in your bloodstream all move the curve — Sections 3 and 4 cover those.

MYTH — "Natural" Substances Are Always Safer

FACT — Organic origins do not dictate a substance's safety profile or its potential for harm. The same pharmacology applies to natural substances as to synthetic ones.

MYTH — “Once You Try It, You're Hooked”

FACT — While highly addictive substances can cause rapid physical dependence, addiction is a complex interplay of biology, environment, and psychology, rather than a guaranteed, immediate result of a single exposure. Many experts categorize substance use disorder (SUD) as a chronic medical condition often triggered by underlying trauma or mental health struggles.

MYTH — “Prescription Drugs are Safer than Illicit Drugs”

FACT — “Many people perceive prescription drugs (such as opioids, stimulants, or benzodiazepines) as "safe" simply because a medical doctor originally prescribed them. However, taking a medication without a prescription or in a way it wasn't intended alters brain chemistry just as powerfully as street drugs. The same pharmacology applies to all drugs.

MYTH — “Craving a redose is due to how you ingested the drug”

FACT — “While the route of administration significantly influences the speed of onset and the intensity of the "high", the underlying compulsion to redose stems from how the substance fundamentally alters brain chemistry and the reward pathway”

Section 2: The Timeline — The 5 Half-Life Rule

Dose decides how high you get. Timing decides how long it lasts — and timing is where most bad decisions happen, because your feelings lie to you about the clock.

The timeline is also important if you want to understand how long to wait before you get tested, and how long to wait before taking a drug after stopping any other medication. There is one simple rule - wait at least 5 half-lives.

Not just skip your usual medication for a day, drink more water, have vitamin C, exercise, etc.

Find out the half-life of your drug and times that number by 5.

2.1 What a Half-Life Actually Is

A **half-life** is the time your body needs to eliminate exactly half of the drug circulating in your blood. Not half the effect — half the substance.

Your liver and kidneys don’t remove a fixed amount per hour; they remove a fixed **proportion**. Take 100 mg of a drug with a four-hour half-life and the countdown looks like this:

100 mg taken	After 4 h	After 8 h	After 12 h	After 16 h	After 20 h
Left in your blood	50 mg	25 mg	12.5 mg	6.25 mg	≈ 3 mg

After **five half-lives**, around 97% of the dose is gone — the practical definition of “cleared”. That’s the **5 Half-Life Rule**, and it holds for every drug and every person. The only thing that changes from drug to drug is how long one half-life is.

> **THE GUIDE’S NOTE**
>
> The tail is long by design. Halving never quite reaches zero on paper — which is exactly why the rule sets the finish line at five cycles, not at “all gone”. Five half-lives clears roughly 97 % of the parent drug for most people and most substances. It is a reliable practical rule of thumb, not a biological absolute. Multi-compartment distribution, active metabolites, impaired liver or kidney function, and individual genetic differences can all leave more residual drug than the simple calculation suggests. If you need to be certain for testing or medical reasons, wait six or more half-lives, or confirm with a reliable source for that specific substance. If you redose, the half-life clock resets from the time of your second dose.

2.2 The High Ends Long Before the Drug Leaves

Here’s the trap: **the high and the half-life run on completely different clocks.** The felt effects fade as the initial surge across the blood-brain barrier levels off and your receptors begin adapting — often within a fraction of one half-life. The substance itself, meanwhile, is still very much on board.

Panel A below shows it plainly: by the time you feel “basically sober”, the majority of the dose may still be circulating in your blood.

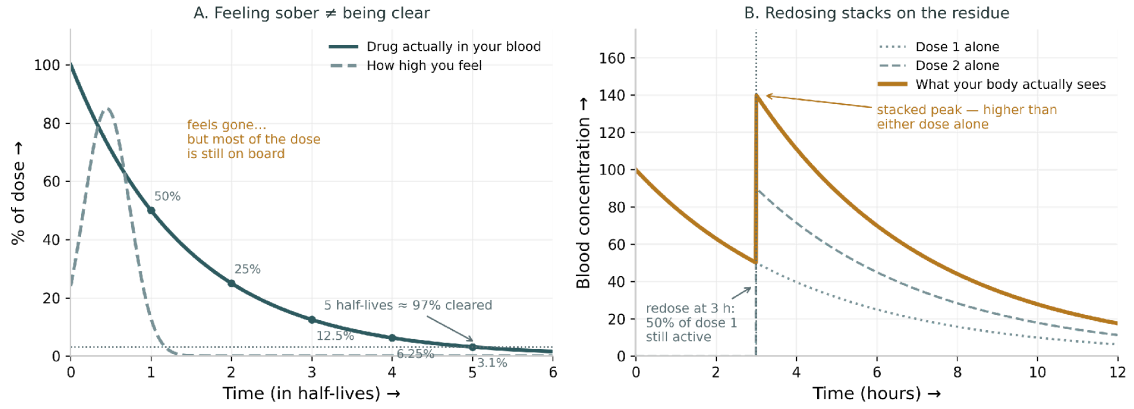

Figure 3 — (A) the felt high ends long before the drug clears; (B) redosing stacks a new dose on top of the old residue (conceptual illustration, half-life = 3 hours).

Perceived sobriety is a feeling. Clearance is a measurement. Most redosing mistakes happen inside the gap between the two.

2.3 The Stacking Problem: Why Redosing can be Dangerous

Run the numbers. A drug with a three-hour half-life: you take a dose at 9 pm. At midnight the sparkle has faded, so you take another. But **50% of the first dose is still active** — the second dose lands on top of it,

and your blood concentration peaks at roughly one and a half times what you planned (Panel B above). A third top-up stacks higher still.

Worse, the math is rigged against you twice. With many drugs the euphoric effects fade faster than the toxic ones, so each redose buys **less high at a higher physical cost** — the plateau effect from Section 1, compounding with the same-day tolerance described in Section 4.2.

> **RULE OF THUMB**
> Decide your total for the session before it starts — then respect the onset time. If you swallow it, wait the full window (up to 90 minutes) before judging. "I don't feel it yet" is not a measurement.

2.4 Half-Lives Vary Wildly

Half-lives range from minutes to days. GHB clears in about 30–60 minutes. Cocaine in roughly an hour. Heroin converts to morphine within minutes. Diazepam lingers for 20–100 hours. Fat-soluble THC metabolites can be detectable for weeks (Section 3.1 explains why).

You **cannot feel** a half-life — a long one feels exactly like a short one. It has to be looked up, which makes it the fifth number to know alongside the four pillars from Section 1.2.

The same rule explains drug tests: they don't detect the high, they detect what's left. A substance can stop affecting you long before it stops being findable.

MYTH — "I feel fine, so it's out of my system."

FACT — Feeling is not measuring. Five half-lives is the measure — and you can't feel those.

MYTH — "The high was short, so the drug must clear fast."

FACT — Not necessarily. Some drugs stop being felt quickly yet circulate for days — and some are converted by the liver into active metabolites that outlast the original compound (see Section 3.4).

> **THE GUIDE'S NOTE**
> Half-life figures usually refer to the parent drug. Some drugs are converted by the liver into active metabolites that stay in the body longer and continue to produce effects or show up on tests. In those cases the parent-drug half-life understates how long the substance remains active or detectable. Always check whether a drug has active metabolites when you look up its clearance time.

2.5 The Urge to Redose

Pharmacokinetics directly dictates the initial intensity of drug cravings by controlling the speed, magnitude, and decline of dopamine release in the brain. The faster a drug reaches the brain, the more

intensely the reward pathway is reinforced, creating a powerful psychological drive to replicate the experience.

Here is exactly how absorption speed, delivery routes, and blood concentration levels shape the urge to redose.

The Speed-to-Brain Relationship: The time it takes a substance to cross the blood-brain barrier determines the intensity of the initial neurochemical spike. Rapid onset causes a sudden, massive surge of dopamine. Slow onset allows the brain to adapt, yielding a gradual dopamine rise.Intense spikes trigger profound euphoria, which the brain encodes as a high-priority survival cue

Route of Administration Dynamics

Different ingestion methods alter the drug's pharmacokinetic profile, directly impacting its addictive potential and the subsequent urge to redose

Inhalation/Smoking: Vaporized drugs pass instantly from the lungs into arterial blood, traveling directly to the brain. This produces an immediate, explosive "rush" and an equally sharp crash, leading to rapid, compulsive cravings to redose.

Intravenous Injection: Injecting a drug directly into the bloodstream bypasses protective barriers, delivering 100% bioavailability almost instantly. The immediacy of the reward heavily reinforces the psychological trigger to use again.

Insufflation/Snorting: Absorption through the nasal mucous membranes is relatively fast but delayed compared to smoking or injecting, leading to a strong but slightly less abrupt craving cycle.

Ingestion/Oral: Swallowed substances must pass through the digestive tract and liver (first-pass metabolism). The slow, gradual climb in blood concentration rarely produces a "rush," resulting in significantly weaker immediate cravings to redose compared to fast-acting routes.

The Half-Life and Crash Cycle: Pharmacokinetics also governs how fast a drug leaves the body. A rapid decline in blood concentration levels drastically intensifies the immediate drive to redose.

Section 3: The Mechanics — How Your Body Processes Drugs

Your body is a series of chemical barriers. How a drug crosses them depends on two things: what the molecule dissolves in, and which door you bring it in through. Change the route, and you change the drug’s entire behaviour.

3.1 Solubility: Fat-Soluble vs Water-Soluble

Every drug molecule is either **lipophilic** (fat-soluble) or **hydrophilic** (water-soluble). This one property dictates how fast a drug hits you and how long it lingers.

- **Water-soluble (hydrophilic).** Dissolves instantly in blood plasma and mucous membranes, hits fast — and is rapidly filtered out by the kidneys. **The danger:** because it clears quickly, it produces a sharper "crash", which drives a strong temptation to redose (e.g. cocaine, 4-MMC).
- **Fat-soluble (lipophilic).** Crosses the blood-brain barrier — which is made of fat — with ease, causing rapid mental effects; but excess molecules get trapped in body fat. **The danger:** it slowly leaks back out over days or weeks. Even when you feel completely sober, the drug is still physically present (e.g. THC, diazepam).

3.2 Bioavailability: The Ultimate Gatekeeper

Bioavailability is the exact percentage of a drug that successfully enters your bloodstream unchanged.

- **The rule of 100%:** only intravenous (IV) injection has 100% bioavailability. Every other method forces the body to destroy a percentage of the drug before it ever reaches your brain.
- **Why it matters:** if a drug has 20% oral bioavailability and 80% nasal bioavailability, snorting the exact same milligram weight makes it roughly four times more potent. A dose that was comfortably swallowed can be dangerous through a different door.

3.3 Routes of Administration: The Four Main Paths

Path A: Swallowed (oral / "bombing")

- **The journey:** stomach → intestines → liver (via the portal vein) → bloodstream.
- **First-pass metabolism:** the liver's security gate. It aggressively breaks down oral drugs before they reach your brain (full story in 3.4).
- **The curve:** long onset (30–90 minutes), smooth and extended peak, gentle comedown.
- **The reality:** the lowest peak toxicity of any route — but the slow onset causes the classic oral overdose pattern: redosing at 40 minutes because "it isn't working yet", right before both doses arrive.

Path B: Snorted (insufflation / nasal)

- **The journey:** mucous membranes → capillaries → bloodstream.
- **The bypass:** this route skips the digestive system and the liver's first-pass metabolism entirely.
- **The curve:** fast onset (a few minutes), steep and intense peak, rapid crash.
- **The reality:** the rapid dopamine spike carries a higher dependency risk, and corrosive compounds (like 4-MMC or ketamine salts) physically damage nasal tissue over time — they trap moisture and alter local pH levels.

Path C: Smoked (inhalation)

- **The journey:** lungs (alveoli) → pulmonary veins → heart → brain.

- **The expressway:** the fastest route to the brain — seconds, beating even IV injection. It bypasses the liver entirely.
- **The curve:** instant onset, explosive peak, immediate drop-off.
- **The reality:** the fastest way to trigger structural changes in brain chemistry, making it the highest-risk route for compulsive patterns of use.

Path D: Rectal ("boofing" / "plugging")

Yes, people do it — and no, it isn't new; suppositories have been a legitimate medical route for centuries. The rectal lining is thin and dense with blood vessels, which makes this route far more efficient than most people assume. That efficiency is exactly why it deserves the same respect as any other path.

- **The journey:** rectal mucosa → capillaries → bloodstream.
- **The partial bypass:** the lower part of the rectum drains straight into the systemic bloodstream, while the upper part drains to the liver first. So you skip *some* of the first-pass metabolism — not all of it, but enough that bioavailability runs noticeably higher than oral for most substances.
- **The curve:** moderate onset (roughly 10–30 minutes — slower than snorting, clearly faster than swallowing), a strong peak, and a duration somewhat shorter than oral.
- **The reality — dose translation:** because more of the drug reaches your blood, **a comfortable swallowed dose can be an overdose taken rectally.** When switching to this route, start far lower than the oral figure — not at it.
- **The reality — tissue and hygiene:** rectal tissue is delicate and tears easily, and caustic powders burn and irritate it. Any tear raises the risk of infection, including STIs. The harm-reduction basics: dissolve fully in sterile water, use a clean oral syringe (never a needle), use lubricant, go gently — and never share equipment.

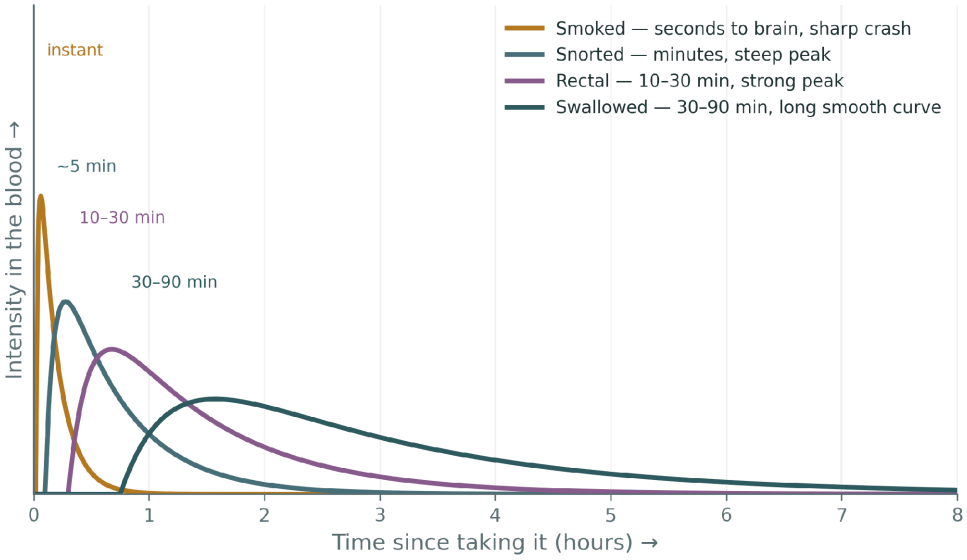

Figure 4 — Same milligrams, different universe: how the route reshapes onset, peak, and duration (conceptual illustration).

The routes side by side:

Route	Onset	The curve	Bioavailability	The catch
Swallowed	30–90 min	Slow rise, long smooth peak, gentle comedown	Reduced — the liver takes the first cut	Lowest peak toxicity; the “it’s not working” redose is the classic trap
Snorted	A few minutes	Steep spike, intense peak, rapid crash	Higher than oral — liver bypassed	Fast dopamine spike raises dependency risk; corrosive to nasal tissue
Rectal	10–30 min	Strong peak, somewhat shorter than oral	Higher than oral — liver partially bypassed	Oral doses do NOT translate — start far lower; delicate tissue, infection risk if torn
Smoked	Seconds	Instant explosive peak, immediate drop-off	High — straight from lungs to brain	Fastest route to compulsive use patterns
Injected (IV)	Seconds	Full spike — everything, all at once	100% by definition	Highest overdose and infection risk; a dose can never be taken back

3.4 The Liver Level: Processing vs Bypassing

The liver is your body’s primary chemical processing plant. How a drug enters your body decides whether it faces the liver’s full defence system immediately — or hits your brain completely untouched.

The liver patrol: first-pass metabolism

Swallow a drug and it doesn’t go straight to your heart or brain. It’s absorbed through the stomach and intestinal walls into a highway of veins called the **hepatic portal system**, which leads directly into the liver.

- **The enzyme factory:** the liver uses specialised proteins called **Cytochrome P450 (CYP450) enzymes** to break down foreign molecules.
- **Deactivation:** the enzymes chop drug molecules into “metabolites” — mostly water-soluble waste your kidneys can flush out in urine. This drastically lowers the amount of active drug that ever reaches your brain.
- **Active metabolites (the exception):** sometimes the liver chops a drug into something stronger than the original — it converts codeine into morphine, for example. This is also why some people get unexpectedly powerful effects from standard doses (see enzyme genetics, Section 4.1).

Bypassing the liver: the raw ingestion paths

Snort, smoke, or inject a drug and you bypass the hepatic portal system entirely. The drug enters capillary beds or lung tissue and goes straight into the systemic bloodstream, heading directly for the heart and

brain. (Rectal use sits in between — roughly half the rectum's blood supply drains through the portal vein to the liver first, the rest goes straight to the heart.)

	Processed by liver first (swallowed)	Bypassing the liver (snorted / smoked)
Blood concentration	Rises slowly; lower overall peak.	Spikes violently; maximum possible peak.
Enzyme defence	High — enzymes destroy a large % of the drug before it reaches the brain.	Zero initial defence — 100% of the absorbed drug hits the brain unchanged.
Duration of action	Longer — the liver metes the drug out over hours.	Shorter — the whole dose lands at once and wears off fast.
Toxicity risk	Lower acute toxicity, but sustained metabolic strain on the liver.	High acute toxicity — the shock to heart and brain lands before the liver can help.

The catch: the liver always wins

Bypassing the liver does not mean escaping it. Once the drug leaves your brain, the bloodstream keeps circulating it — and every pass through the liver, the enzymes chop away a little more. Bypassing simply delays the processing, allowing the drug to hit your brain with full, unprotected force on its very first pass.

Section 4: The Environment — The Individual and the Cocktail

Even a perfectly calculated dose doesn't land in a vacuum. It lands in a specific body, with a specific history, possibly sharing the bloodstream with other chemicals. This section is about why a dose that's fine for one person can be dangerous for another — and why mixing changes the arithmetic entirely.

4.1 Individual Biology: Why One Size Never Fits All

- **Body mass and composition.** Standard dosing guides assume a baseline body weight (typically a 70 kg / 154 lb male). A larger body volume dilutes a drug across more tissue: give a 100 kg person and a 50 kg person the same milligram dose of a water-soluble drug, and the 50 kg person experiences roughly double the blood concentration.
- **Enzyme genetics.** Genetic variations change how many CYP450 enzymes your liver produces. "Poor metabolisers" can't break a drug down fast enough, so it builds to toxic levels quickly. "Ultra-rapid metabolisers" clear it so fast they barely feel it — and often take dangerous amounts chasing the effect. Same dose, opposite problems.
- **Pre-Existing Health Conditions.** Your body's current health changes how it handles substances.Heart Issues: If you have high blood pressure or a heart condition, stimulants pose a much higher risk of heart failure.

- **Liver or Kidney Damage**. If your liver or kidneys aren't working well, your body cannot break down or get rid of substances. This causes them to build up to toxic, deadly levels in your system much faster.
- **Mental Health Conditions**. Substances can severely worsen underlying anxiety, depression, or psychosis.

4.2 Tolerance vs Tachyphylaxis

Your brain actively fights back against foreign chemicals to maintain equilibrium (homeostasis). It does this on two very different timescales:

- **Downregulation (standard tolerance).** With repeated use over weeks or months, the brain physically removes or hides its own receptors so the drug has fewer places to land. You must continuously increase the dose to get the same effect — while the toxic dose stays exactly where it was.
- **Tachyphylaxis (rapid short-term tolerance).** A sudden, aggressive tolerance that can build within hours, or after a single dose. Psychedelics like LSD or psilocybin, and certain monoamine releasers like 4-MMC, can cause rapid receptor saturation: redosing a few hours later often yields zero extra euphoria while doubling the physical toxicity and body-temperature strain.

Both mechanisms produce the same trap: **the dose that works keeps rising, but the dose that harms doesn't move.**

4.3 Polysubstance Dynamics: The Danger Matrix and Contraindications

Mixing drugs doesn't just add their effects together (1 + 1 = 2). Combinations can multiply effects exponentially (1 + 1 = 5) or — just as dangerous — mask what's actually happening in your body. There are three patterns worth knowing about..

Type A: Synergistic depressants — the suffocation trap

The mix: alcohol + benzodiazepines, or opioids + alcohol / benzos. **The mechanic:** both drugs slow the central nervous system through different pathways, and together they can switch off the brainstem's automatic signal to breathe. This combination pattern is the leading cause of accidental drug fatalities — and it requires no exotic substances, just common ones meeting.

Type B: Overlapping stimulants — the cardiac strain

The mix: cocaine + amphetamines, or 4-MMC + MDMA. **The mechanic:** both drugs spike blood pressure and force the heart to beat faster while narrowing the blood vessels (vasoconstriction) — more demand, less supply. The risk of stroke, heart attack, or lethal overheating (hyperthermia) rises sharply.

Type C: Antagonistic masking — the illusion of sobriety

The mix: stimulants + alcohol (cocaine or 4-MMC + drinks). **The mechanic:** the stimulant masks alcohol's sedating effects, so you feel sober and keep drinking toxic amounts. When the shorter-acting stimulant

wears off, the full alcohol load hits at once — sudden, acute alcohol poisoning. A chemical footnote makes this specific mix worse: when cocaine and alcohol meet in the liver, the body synthesises **cocaethylene**, a third compound more toxic to the heart than either parent drug.

The pattern	Classic mixes	What happens	The risk
Synergistic depressants	Alcohol + benzos; opioids + alcohol or benzos	Both slow the CNS via different pathways; effects multiply	The automatic breathing signal can switch off — the leading cause of accidental drug deaths
Overlapping stimulants	Cocaine + amphetamines; 4-MMC + MDMA	Heart rate and blood pressure spike while blood vessels narrow	Stroke, heart attack, or lethal overheating (hyperthermia)
Antagonistic masking	Stimulants + alcohol	The stimulant hides the drunkenness — you feel sober and keep drinking	When the stimulant wears off, the full alcohol load hits at once: sudden alcohol poisoning

Interactions are one of the few risks you can check in advance, sober, in about two minutes.

4.3 Understanding MAOIs (Monoamine Oxidase Inhibitors)

One of the biggest issues on public forums is the understanding around MAOIs (Monoamine Oxidase Inhibitors). Mainly from people who have taken a drug while also taking prescribed Monoamine Oxidase Inhibitors and didn't have any negative effects. So they assume because they were OK you will be ok. This simply is not true.

The simple fact is that MAOIs are highly dangerous when mixed with illicit drugs.

This combination can cause a fatal spike in blood pressure or a toxic overload of brain chemicals.

Why MAOIs are Dangerous

MAOIs work by blocking an enzyme that cleans up brain chemicals like serotonin, dopamine, and norepinephrine. Because this cleanup system is turned off, adding illicit drugs that stimulate the brain creates a massive, uncontrolled buildup of these chemicals.

Illicit Drug	Main Risk	What happens
MDMA (Ecstasy/Molly)	Serotonin Syndrome	Deadly buildup of serotonin; causes extreme fever, seizures, and muscle breakdown.
Cocaine	Hypertensive Crisis	Massive spike in norepinephrine; causes stroke, heart attack, or ruptured blood vessels.
Amphetamines / Meth	Hypertensive Crisis	Extreme release of dopamine and norepinephrine; causes sudden, fatal spikes in blood pressure.

Illicit Drug	Main Risk	What happens
Psychedelics (LSD, DMT, Ayahuasca)	Neurotoxicity	Unpredictable, severe psychological distress and dangerous spikes in heart rate and blood pressure.
Opioids (especially Heroin, Fentanyl, Tramadol)	Respiratory Failure / Death	Tramadol causes serotonin syndrome; other opioids heavily increase the risk of fatal respiratory depression.

Critical Symptoms of a Bad Reaction

Seek emergency medical help immediately if someone on an MAOI takes an illicit drug and experiences: A sudden, severe headacheExtreme sweating or high feverRapid, pounding heartbeatRigid or jerking muscles. Confusion, agitation, or hallucinations.

The Core Problem

The "Off" Switch is Gone. In a normal brain, neurotransmitters like serotonin, dopamine, and norepinephrine are released, do their job, and are quickly destroyed by an enzyme called Monoamine Oxidase (MAO).

MAOIs completely deactivate this enzyme. When you take an MAOI, your brain's natural "cleanup crew" is offline. If you introduce an illicit drug on top of this, the results are catastrophic because the brain has no way to clear the chemical surge.

The Two Deadly Mechanisms.

Serotonin Syndrome (The Overheating Brain)

The Culprits: MDMA, Tramadol, and certain psychedelics (like Ayahuasca/DMT).

The Science: MDMA forces the brain to flood its receptors with serotonin. Normally, MAO would break this excess down. Under an MAOI, the serotonin just keeps piling up.

The Result: The body's thermostat breaks. Internal body temperature can rapidly spike above 41°C (106°F), cooking internal organs, melting muscle tissue into the bloodstream (rhabdomyolysis), causing severe seizures, and leading to organ failure.

Hypertensive Crisis (The Exploding Blood Pressure)

The Culprits: Cocaine, Amphetamines, Methamphetamine.

The Science: Stimulants force a massive release of norepinephrine (adrenaline) and dopamine, while simultaneously blocking their reuptake.

The Result: Because MAO cannot break down this massive surge of adrenaline, blood vessels constrict violently and the heart pumps erratically. Blood pressure spikes so high and so fast that it can cause immediate strokes, ruptured aortas, or fatal heart attacks.

The "Washout" Period Danger

The danger doesn't stop when a person stops taking their medication.

Irreversible Inhibition: Most classic MAOIs are "irreversible." They permanently destroy the MAO enzymes currently in the body.

The Two-Week Rule: It takes the human liver about 14 days to manufacture brand-new MAO enzymes.

The Trap: If someone stops taking an MAOI on Monday and takes MDMA or Cocaine on Friday, they are still at full risk for a fatal reaction because their body hasn't rebuilt its clean up enzymes yet.

Section 5: Educate Yourself — Finding the Numbers

Everything so far has told you which numbers matter. This final section is about where to find them, how to check what you actually have, and what to do when things go wrong — the same toolkit harm-reduction professionals use.

5.1 Look It Up Before You Need It

For any substance, five things to know before it goes anywhere near your body:

- **Dose ranges by route** — threshold, common, heavy — and whether the safety margin is wide or razor-thin (Section 1).
- **Onset time for your chosen route**, so “it’s not working” never tricks you into stacking (Sections 2–3).
- **Duration and half-life**, so you know when you’re actually clear — not just when you feel sober (Section 2).
- **Known dangerous combinations**, checked against anything else you take — including alcohol and prescription medication (Section 4).
- **What a bad reaction looks like**, so you recognise it early in yourself or a friend (Section 5.5).

Do this research sober, in advance, and keep a screenshot on your phone. The middle of the experience is the wrong time to start reading.

https://www.drugs.com/ is probably one of the best resources for full information about prescription drugs. See the Annex for half

5.2 Trusted Reference Sources

These are the sources harm-reduction professionals actually use. Cross-check at least two — the numbers should broadly agree.

- **Erowid** (erowid.org) — the oldest and largest archive: dose pages, duration data, and thousands of documented experience reports.

- **PsychonautWiki** (psychonautwiki.org) — standardised dose ranges, duration charts, and interaction notes for almost every known substance.
- **Bluelight** (bluelight.org) — a community-driven platform that provides relevant information and dialogue about drug use and harm reduction.
- **TripSit** (tripsit.me) — combination and interaction charts that map dangerous mixes, plus factsheets and a live help chat.
- **DMT-Nexus** (dmt-nexus.me)— The DMT-Nexus is a prominent online community and forum dedicated to the discussion, exploration, and safe use of N,N-dimethyltryptamine (DMT) and other psychoactive compounds.
- **ARP Consult** (arupconsult.com/content/drug-half-lives-and-urine-detection-windows) — Drug Half-Lives and Urine Detection Windows table provides estimates for drug detection in plasma and serum specimens.

5.3 Test What You Have

In unregulated markets, purity and contents are unknown. “Same stuff as last time” is an assumption, not a fact — batches vary, and adulterants are common. Testing removes one specific unknown: what’s actually in the bag.

- **Reagent test kits** — cheap colour-change drops that indicate whether the expected compound is present and flag common substitutions. A first filter, not proof.
- **Fentanyl test strips** — small strips that detect fentanyl contamination in powders and pills within minutes. Given fentanyl’s microscopic lethal dose, this is the single highest-value test for anything bought as powder or tablets.
- **Lab drug-checking services** — where legal, anonymous services analyse a sample and tell you exactly what it contains and how strong it is. The gold standard. Google is your friend here.

> **KEEP IT HONEST**
> Testing can’t make a drug safe — nothing can. It makes a drug known, which is a very different starting position from guessing.

5.4 Weigh, Don’t Eyeball

Eyeballing powder is guessing. A “line” or a “bomb” can vary tenfold depending on how fine the powder is and how heavy the hand. For anything measured in milligrams, the only honest tools are:

- **A milligram scale (0.001 g)** — inexpensive, and the minimum standard for weighing powders. Essential for any substance with a narrow therapeutic index.
- **Volumetric dosing** — for substances active in tiny amounts: dissolve an exactly weighed amount in an exactly measured volume of liquid, then measure individual doses by millilitre. It turns microgram-range substances into something you can actually measure.

- **Your own measurements** — never trust someone else's "it's about 100 mg". Their scale, their crush, and their guess are not yours.

5.5 When Something Goes Wrong

No judgement here either: emergencies happen to experienced people too. Knowing the red flags in advance is what turns a bad night into a story instead of a statistic.

Recognise the red flags:

- **Depressants (opioids, GHB, benzos, alcohol):** slow or stopped breathing, blue or grey lips, can't be woken. This is always an emergency.
- **Stimulants (cocaine, amphetamines, MDMA, 4-MMC):** chest pain, a body temperature that won't come down, seizures.
- **Serotonin syndrome (serotonergic combinations):** very high temperature, rigid muscles, agitation, confusion — most often after mixing MDMA-type drugs with certain antidepressants, or with each other.

Know what to do:

- **Call emergency services immediately**, and say what was taken if you know — medics treat, they don't lecture. Many regions have Good Samaritan protections for people who call for help.
- **If they're breathing but unresponsive:** recovery position — on their side, so vomit can't choke them — and stay with them.
- **If opioids could be involved:** naloxone can reverse an opioid overdose and is available without a prescription in many countries. If opioids are anywhere in your circle, carrying it is a no-brainer.
- **If overheating:** move somewhere cool, loosen clothing, cool the neck, armpits and groin with whatever's available, and sip — don't chug — water.
- **Never** let someone "sleep it off" with depressants on board, and never leave them alone.

> **THE TAKEAWAY**
> Knowledge is the only safety equipment you carry everywhere. Learn the numbers. Check the substance. Respect the timeline. Then pass it on — the best harm reduction is shared.

Glossary: The Terms in Plain Language

Every technical term used in this guide, translated. If you remember nothing else, remember where this page is.

Term	What it means in practice
Bioavailability	The percentage of a dose that actually reaches your bloodstream, unchanged.
Blood-brain barrier	The fatty filter between blood and brain; only certain molecules can cross it.
Boofing / plugging	Slang for rectal administration — an efficient route that demands lower doses than swallowing.
CYP450 enzymes	The liver proteins that chop drug molecules into removable pieces.
Dose-response curve	The S-shaped graph of how effects change as the dose increases.
Downregulation	The brain hides or removes receptors after repeated exposure — the basis of tolerance.
ED50	The dose at which 50% of people get the desired effect.
First-pass metabolism	The liver's pre-filtering of anything swallowed, before it reaches the brain.
Half-life	The time needed for your body to eliminate half of what's in your blood.
Hepatic portal system	The vein highway that routes everything absorbed from the gut through the liver first.
LD50	The statistically calculated dose that is lethal to 50% of a test population.
Metabolite	What a drug molecule becomes after the liver processes it — usually waste, sometimes stronger.
Onset	The time between taking a drug and feeling the first effects.
Polysubstance use	Taking more than one drug in the same session — including alcohol.
Tachyphylaxis	Sudden same-day tolerance: redosing adds toxicity but no extra effect.
TD50	The dose at which 50% of people experience a severe side effect.
Therapeutic index	The gap between an effective dose and a dangerous one — wide, or razor-thin.
Threshold dose	The smallest amount that produces any noticeable effect.
Tolerance	Needing more of a drug over time to get the same effect.
Vasoconstriction	Narrowing of blood vessels — raises blood pressure and strains the heart.
Volumetric dosing	Dissolving a known weight in a known volume of liquid to measure tiny doses accurately.

Support an old Raver

This guide is entirely free, open-source, and ad-free to ensure public access to accurate, science-based health data. If this breakdown of pharmacology, half-lives, and dose-response dynamics helped you make safer, more informed decisions, consider dropping an anonymous tip to support an old raver..

Option 1: Monero (XMR) — 100% Globally UntraceableMonero is a privacy-first cryptocurrency. Transactions completely hide the sender, receiver, and the amount sent.

Raw Wallet Address:
86YFZ1Sp2GaaGRWQtYKpWKLQn5pZVQWcSUKVAMFCs4F2BvL4yeA3gP7ZbfHKdphCEqckB8jJ99emxj45AFPg3TbQAvC74Ck

Option 2: Bitcoin (BTC) — Most AccessibleBitcoin is widely supported on common exchange apps (Cash App, Coinbase, Kraken). Please note that while your identity is hidden from me, Bitcoin uses a public ledger.

Raw Wallet Address:bc1qksyam36r77vc0j9p325u6pqdnaxjhry2q62p53

Pass it on.

The best harm reduction is shared knowledge.