

Introduction

Definition

toxikos (poison) +
logos (study)

toxic: a chemical
substance that creates
an alteration

Xenobiotic: foreign
chemical that can cause
harm to living organisms.

food toxicology: study
of xenobiotics' toxic
effects in human and
animal food

History

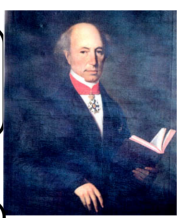
It started with the
use of plants

Assassination,
poisoning and
warfare



Paracelsus: "the dose
makes the poison"

Orfila i Rotger →
founders of Modern
Toxicology



Bernardino
Ramazzini → father
of work toxicology

new discoveries
during World Wars

Arnold Lehman →
FDA founder



Sciences

basic (analytical
or experimental)

applied
forensic
clinical
environmental
occupational
food
veterinary
medical
drug addiction
organ-specific
regulatory

Toxicity

intrinsic quality of a substance, it
depends on biotransformation,
defense, physiology and
chemicals ratios

Toxicity
potential

Risk

probability of
creating toxicity

risk
epidemiological
studies

dose/effect
ratio

damage and
concentration
comparison

dose/response
ratio (population)

hypo- and hyper-
sensitive

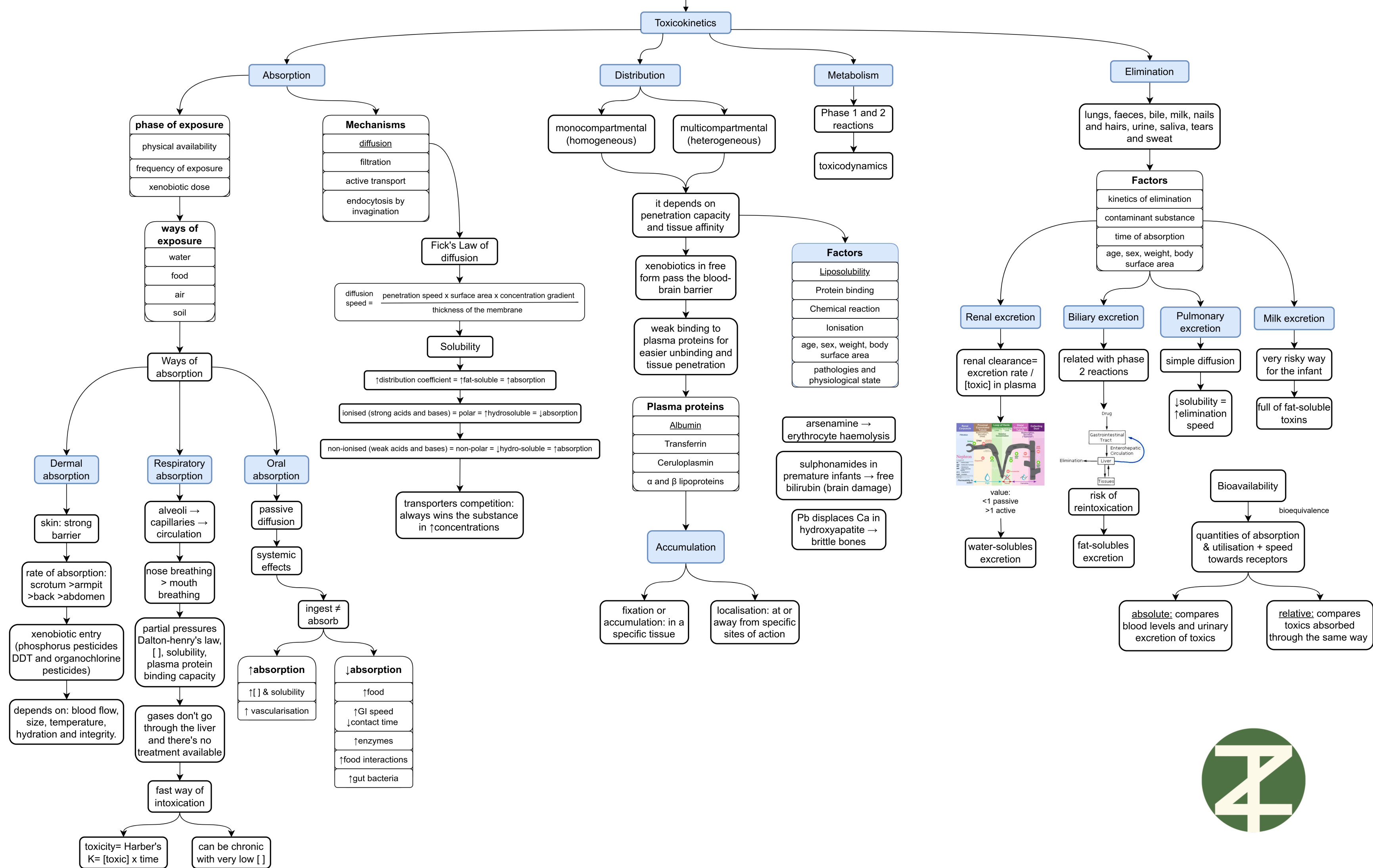
Gauss bell

Hormetins

toxicity due to
deficit of excess

benefits in
small doses







Toxicodynamics

biotransformation:
make a xenobiotic
more polar

Factors

genetics: accumulation,
prolongation,
hypersensitivity

species: qualitative P2R,
quantitative P1R

sex, diet, environment

Phase 1 reactions

oxidation, reduction and
hydrolysis reactions

they create (active)
polar groups

Oxidation

microsomal

+1 oxygen atom
water creation
CYP450
↑polarity

non-
microsomal

hydroxylations OH
aliphatic, alicyclic,
aromatic

epoxylations O₂
adduct = covalent

dealkylations
→ remove alkyl group

oxidative deamination
→ aromatic + amine =
hydroxylation

oxidative dehalogenation
→ remove halogens from
the molecule

amines oxidation:
monoamine or
diamine oxidase
(histamine)

oxidation of alcohols
and aldehydes
(dehydrogenases)

Reduction

capture of
electrons

enzymes with
nitro or azo
groups

Nitro: anaerobic
conditions, NADH,
nitrobenzene →
aniline

azo dyes →
azo reductases
→ 2 amines

Hydrolysis

no energy
required

xenobiotics
with ester or
amide bond

esterases →
acid + alcohol

amidases →
acid + ammonia

Phase 2 reactions

conjugation reactions

they create inactive
polar groups

they act after P1R to
ensure molecule polarity

transferase enzymes +
donor agent + energy

type 1 activated
conjugating agent

conjugation with
glucuronic acid (+UDP)
and oxygen structure

conjugation with
sulphate anion (+PAPS)
and OH groups

conjugation with methyl
groups (+SAM) and aromatic
amines, phenols and thiols

conjugation with acetyl
groups (+Acetyl-CoA)
and aryl amines

conjugation with glutathione
(LGLCG) and halogenated
compounds

type 2 activated
substrate (aa's)

conjugation with amino
acids and xenobiotics
with carboxyl groups

acid-CoA-ligase enzyme and
n-acetyl-transferase enzyme

elimination
through urine

