

Poisons

“Any substance which, if taken into or formed in the body, destroys life or impairs health.”

Paracelsus

Philippus Aureolus Theophrastus
von Hohenheim (1493 – 1541)

First to think scientifically
about poisoning

Medicinal chemist



Paracelsus

Paracelsus

“All substances are poisons, there is none which is not a poison. The right dose differentiates a poison from a remedy.”

Even water

Lethal water

Water poisoning



Over 7 litres



Lethal dose

KDND, Sacramento, California

“Hold Your Wee For a Wii”

See how much water people can drink

Winner wins Wii game station

KDND, Sacramento, California

Drank about 7.5 L of water

Went home, became unwell and died

Family compensated U.S. \$16 million



Jennifer Strange

KDND, Sacramento, California

Jennifer Strange placed second

"I didn't know what was wrong with me. I just knew I had never felt so sick in my life."
- Winner of contest, Lucy Davidson



Foxgloves

Fox glove

Poisonous European wild plant

Contains digitalin



Potent heart muscle stimulant

Over-consumption leads to death

Digitalin

Also used clinically



Failing heart



Give controlled dose of digitalin



Heart beats properly

Dose-Response

Steepness of the curve



Variable

How to measure toxicity?

DNA

Fingerprints

Fibre Analysis

Poison

Blood

Measuring toxicity: LD₅₀

Lethal dose for 50 percent

Amount of chemical required to kill half of the test population

Measuring toxicity: LD₅₀

Lethal dose for 50 percent

Amount of chemical required to kill half of the test population

How accurate is LD₅₀?

Accuracy of LD₅₀

1 Vary according to administration of poison



Oral administration vs direct injection

Accuracy of LD₅₀

1 Vary according to administration of poison

2 Depend on species used for testing



Typically mice or rats



Assume similar LD₅₀ values for humans

Accuracy of LD₅₀

Lethal dose for 50 percent

Amount of chemical required
to kill half of the test population

How accurate is LD₅₀?



Guidelines

Lethal doses

Types of poison	Lethal dose ($\mu\text{g} / \text{kg}$), mice
Sodium cyanide	10 000
Curare/ strychnine	500
Tetrodotoxin	8 – 20
Cobra neurotoxin	0.3
Tetanus toxin	0.07
Botulism toxin	0.03

Measure dose
per unit body
weight

Factors affecting LD₅₀

1 Size



Larger doses for larger bodies (mg/ kg)

2 Age



Metabolism changes with age

3 State of health



Liver condition

Factors affecting LD₅₀

4

History



Build up and loss of tolerance

E.g. heroin addict



Keep increasing dose



Tolerance



Loses tolerance after a long time without heroin

Factors affecting LD₅₀

5

Paradoxical reactions



Rare but known

E.g. anti-malarial medicine Lariam



Side effects



Depression

Factors affecting LD₅₀

Vanessa Brunt



Went to South China



Took Larium



Became very depressed



Committed suicide