

CLINICAL APPLICATION OF UNDERSTANDING MECHANISMS OF ACTION (EXAMPLE)

ELIMINATION OF HYPNOTIC DRUG PHENOBARBITAL (AND OTHER ACID SUBSTANCES) FROM ORGANISM (E.G. OVERDOSING)



Diffusion of a drug across biological membrane – the substance must be non-ionised.

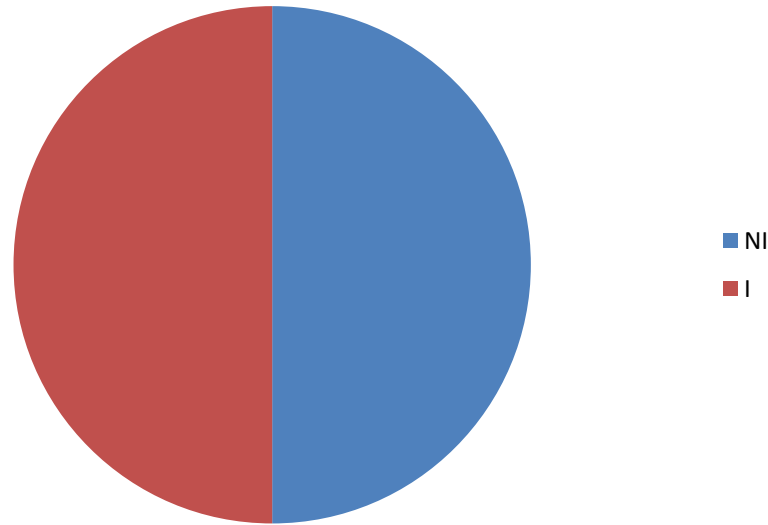
Level of ionisation affect: **dissociation constant of the drug**

pH of environment

DISSOCIATION CONSTANT

- **Constant for each drug**
- **It is not changed owing to factors of environment**
- **Indicated with symbol pK**

Barbiturate hypnotic drug phenobarbital has pK value = 7,5

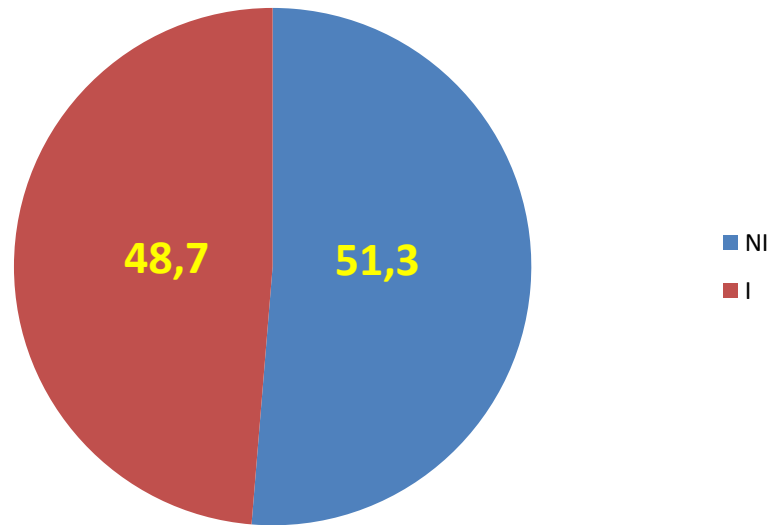


Hypnotic drug phenobarbital has $pK = 7,5$ this means that at $pH = 7,5$ we find 50 % of the substance in the form of ions – ionised (I) and 50 % in the form of molecules – non-ionised (NI).

Phenobarbital is a very weak acid.

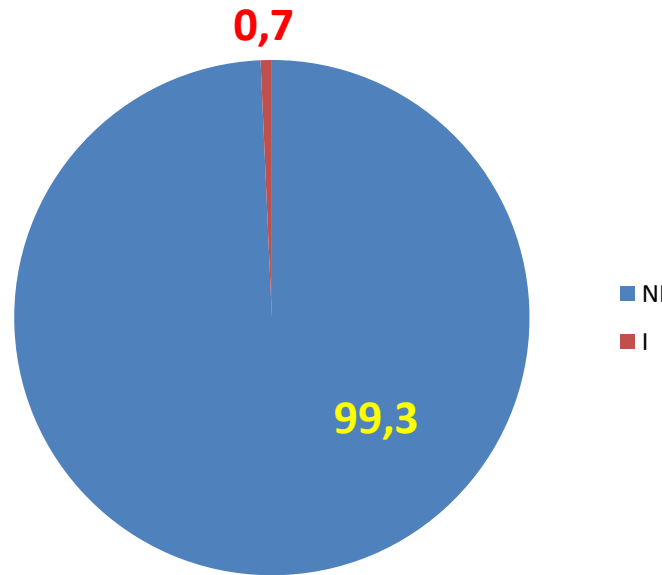
The effect of different pH in organism on phenobarbital dissociation.

BLOOD (pH = 7,4)



The effect of different pH in organism on phenobarbital dissociation.

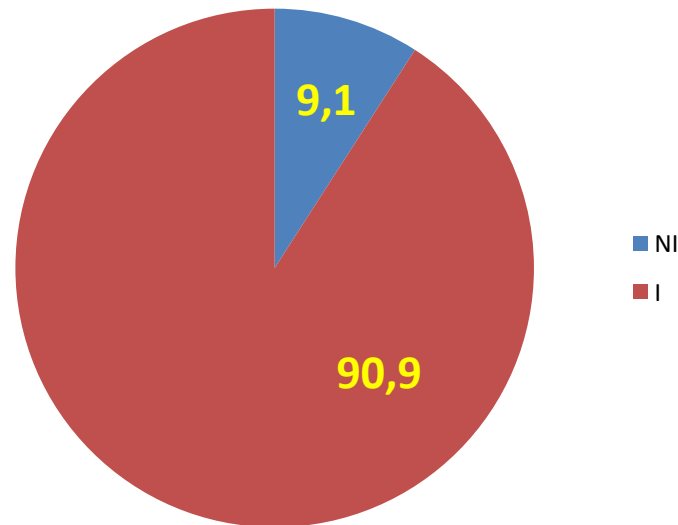
Eliminated to acidic URINE (pH = 5,0)



Acidic substances are in acid solution mainly in non-ionised form.

The effect of different pH in organism on phenobarbital dissociation.

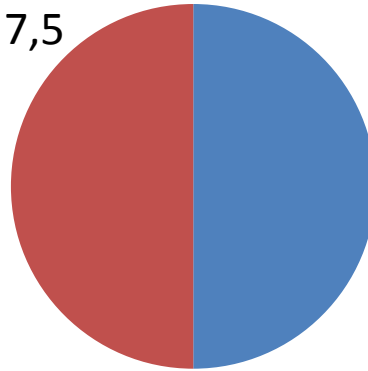
When eliminated to alkaline URINE – shift of urine pH by alcalising substances (pH = 8,5)



Acidic substances are in alkaline solution mainly in ionised form.

Ionised part of the drug does not cross biological membranes by diffusion, because it is not soluble in lipids.

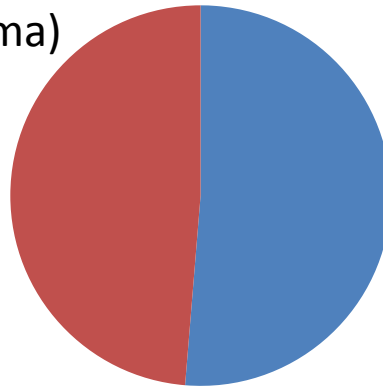
pH 7,5



■ NI

■ I

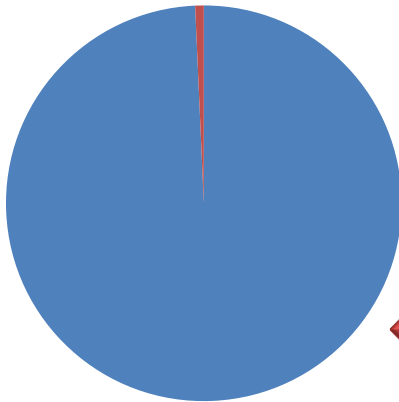
pH 7,4 (blood plasma)



■ NI

■ I

pH 5,0 (acidic urine)



■ NI

■ I

Phenobarbital is eliminated via urine

Usual pH of urine = 5,0



Phenobarbital is immediately converted to almost non-ionised form in urine (99,3 % non-ionised)

Normally phenobarbital crosses biological membranes of kidneys back to the blood stream
and to the brain

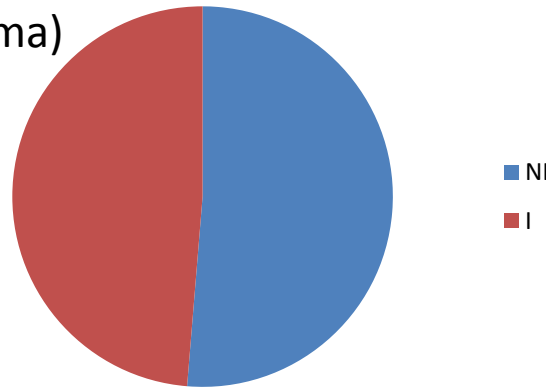
- its sedative effects continues.

**Therapy: acidic substances are in alkaline environment
present mainly in ionised form – they cross the membranes only to very limited extent.**

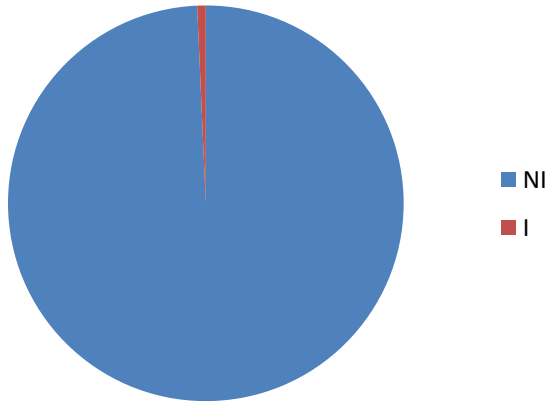
Use of alkalisng substances suppresses reverse resorption in kidneys

Non-ionised part in urine = 9,1 %, ionised part = more than 90 %
- significantly decreased reverse diffusion of phenobarbital.

pH 7,4 (blood plasma)



pH 5,0 (acidic urine)



E.g. NaHCO_3

pH 8,5 (alkalised urine)

