

JULY 2007
QUESTION 12

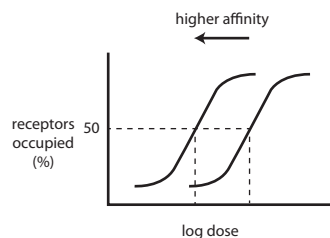
The binding of a drug (D) to a receptor (R) is illustrated by the following expression $[D][R] \xrightleftharpoons[k_{off}]{k_{on}} [DR]$ Explain the following terms;

a) the ratio of k_{off} / k_{on}

This is the dissociation constant (K_d)
It is based on the law mass action

b) the implications of a low value for the above equation

at a low concentration of drug many of the receptors are occupied
it means that the drug binds more tightly to the receptor
represented by the receptors occupied / dose curve being to the left



c) the term affinity

is the inverse of dissociation, a high affinity is associated with a low dissociation constant
can be described via the association constant K_a which is the inverse of K_d .

d) the clinical implications for a high value for affinity

as above, less drug required to occupy 50% of the receptors
bind more tightly to receptors
generally results in higher potency (when there is a graded response to % receptors occupied)

e) Physiological factors which affect the rate constant k

determined by the Arrhenius equation
variables include

- T - temperature is the main factor
- E_A - activation energy may be lowered by addition of a catalyst
- R - the gas constant (derived from $PV=nRT$)
- A - frequency factor