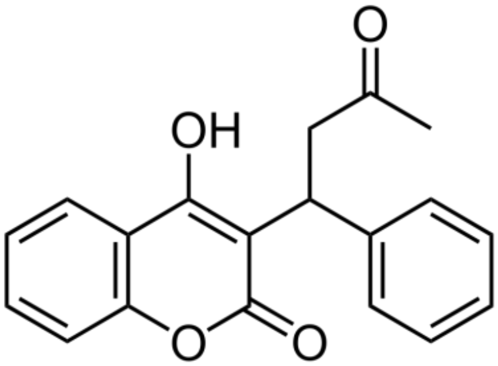
Equilibrium binding of Warfarin

Warfarin binds to human serum albumin (HSA) with a dissociation constant of 3 mM (3×10^{-3} M). Given that HSA has a concentration of 12 mM in blood and warfarin has a concentration of 1.5 μM in a patient, calculate what fraction of warfarin is bound to HSA. (NOTE: 1 μM = 10^{-6} M)

War + HSA ←→ War-HSA



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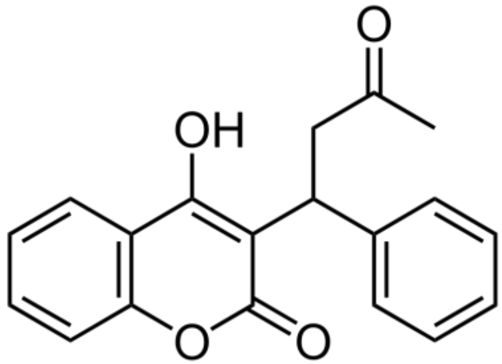

Solution: Make a reaction table

	War	HSA	War-HSA
Initial	1.5×10^{-6}	12×10^{-3}	0
Change	-x	-x	x
Equilibrium	1.5×10^{-6} - x	12×10^{-3} – x	x

Equilibrium binding of Warfarin

In this case we can make the assumption that the concentration of HSA is constant since it has a much greater concentration than Warfarin [HSA] >> [Warfarin]. This makes the equilibrium expression more reasonable and is a very good approximation. Note that we were given K_d, and so we can calculate K_a from K_d. K_a stands for the association constant.

$$K_a = \frac{1}{K_d} = 333$$

The K_a is

$$K_a = \frac{[War - HSA]}{[War][HSA]}$$

Equilibrium binding of Warfarin

When we substitute the values into the association equilibrium constant we have

$$K_a = \frac{x}{(1.5 \text{ x } 10^{-6} - x)(12 \text{ x } 10^{-3})}$$

After some algebra we find x.

$$333(12 \text{ x } 10^{-3}) = \frac{x}{(1.5 \text{ x } 10^{-6} - x)}$$

$$(3.996)(1.5 \text{ x } 10^{-6} - x) = x$$

$$5.994 \text{ x } 10^{-6} = 4.996x$$

$$\text{x} = \frac{5.994 \text{ x } 10^{-6}}{4.996} = 1.2\, x 10^{-6}$$

We conclude that the War-HSA complex is 80% associated.