Material for Electronic Supplement

Derivation of the tissue-gas-film 3 phase resistance model to describe the relationship between thin-film equilibration times and K_{OA}

In this model, the total resistance (R_{TOTAL}) that a chemical substance encounters when diffusing from the sample matrix into the thin film can be represented by the t_{95}. The total resistance can be viewed as the sum of the resistances for mass transport of the chemical in the biological tissue (R_T), the gas-phase (R_G) and the thin film (R_F):

$$R_{TOTAL} = R_T + R_G + R_F \quad (5)$$

Following the fugacity approach, R_{TOTAL} can be represented by the reciprocal of the chemical conductivity, expressed by the film-to-tissue transport parameter D_{FT} (mol.Pa^{-1}.hr^{-1}). D_{FT} is related to the chemical transport parameters in the biological tissue (D_T), the gas-phase (D_G) and the thin film (D_F):

$$1/D_{FT} = 1/D_F + 1/D_G + 1/D_T \quad (6)$$

Chemical transport in the biological tissue and the film is mainly through diffusion. As a result D_F and D_G can be expressed as:

$$D_F = \kappa_F..A._F Z_F \text{ and } D_T = \kappa_T.A_T.Z_T \quad (7)$$

Where κ_F. and κ_T are the mass transfer coefficients (m/hr) for diffusion in the film and tissue respectively; A_F and A_T are the areas of diffusion (m^2) and Z_F and Z_T are the fugacity capacities ($mol.m^{-3}.Pa^{-1}$) of the film and tissue for the chemical.

Chemical transport in the gas phase is through a combination of diffusion and flow generated by rotating the vials. D_G can be expressed as:

$$D_G = Q_G.Z_G \quad (8)$$

Where Q_G is a hypothetical flow rate (m^3/hr), representing diffusion and gas circulation in the vial. Substitution of equation 7 and 8 in equation 6, gives:

$$1/D_{FT} = (1/\kappa_F.A._F Z_F) + (1/ Q_G.Z_G) + (1/\kappa_T.A_T.Z_T) \quad (9)$$

The equilibration time t_{95} can be expressed as :

$$t_{95} = 3/k_{FT} \quad (10)$$

where k_{FT} is the rate constant (hr^{-1}) for film-to-tissue transfer. Following the fugacity approach, k_{FT} can be represented by:

$$k_{FT} = D_{FT}/(V_F.Z_F) \quad (11)$$

where D_{FT} is the transport parameter ($mol.Pa^{-1}.hr^{-1}$) for film-to-tissue transfer. Combining equations 9, 10 and 11, results in:

$$t_{95} = 3.\ (V_F.Z_F)/\ D_{FT} \ = 3.\ (V_F.Z_F).\{(1/\kappa_F.A_F.Z_F) + (1/\ Q_G.Z_G) + (1/\kappa_T.A_T.Z_T)\} \quad (12)$$

which can be simplified to:

$$t_{95} = 3.(V_F.Z_F)/\ D_{FT} \ = \ 3\ .\ \{(d_F/\kappa_F) + (V_F.K_{FG}/Q_G) + (V_F.K_{FT}\ /\kappa_T.A_T)\} \quad (13)$$

where d_F is the thickness of the film, K_{FG} is the film to gas phase partition coefficient (Z_F/Z_G) and K_{FT} is the film to tissue partition coefficient (Z_F/Z_T). Equation 13 illustrates that since K_{FG} is correlated to K_{OA} and K_{OA} varies from $10^{6.3}$ to $10^{9.2}$ for the test chemicals in this study, the gas-phase resistance ($V_F.K_{FG}/Q_G$) can be expected to increase substantially relative to film and tissue phase resistance. K_{FT} representing the film/tissue partition coefficient is not expected to vary substantially among the test chemicals. An increase in film thickness is expected to result in a proportional increase in the overall resistance and hence in the value of t_{95}.