Erratum

Equation (7) of Rowland (1) is in error. This read

$$Cu(m_i)_{ss,po} = \frac{[f_a \cdot R_{o,po} \{E(d)_g \cdot fm_{i,g}(1 - E(m_i)_g) + (1 - E(d)_g) \cdot fm_{i,H}\}](1 - E(m_i)_H)}{CLu(m_i)} \quad (1)$$

where $Cu_{ss}(m_i)_{ss,po}$ is the steady-state unbound concentration of the i th metabolite (m_i) formed following an oral constant rate infusion of drug $R_{o,po}$; $E(d)$, $E(m_i)$ are the extraction ratios of drug and i th metabolite respectively; subscripts g, H refer to gastrointestinal tract and liver, respectively; fm_i is the fraction of drug entering an organ that is converted to m_i , f_a is the fraction of orally administered drug available for passage across the gastrointestinal wall, and $CLu(m_i)$ is the unbound clearance of m_i .

It should have correctly read

$$Cu(m_i)_{ss,po} = \frac{f_a \cdot R_{o,po}(1 - E(m_i)_H)}{CLu(m_i)} [E(d)_g \cdot fm_{i,g}(1 - E(m_i)_g) + fm_{i,H}(1 - E(d)_g)(1 - fe(d) \cdot F_H)] \quad (2)$$

where $F_H = 1 - E(d)_H$, and $fe(d)$ is the fraction of the available drug that is excreted unchanged in urine.

The discrepancy arose in the derivation of the rate of presentation of the i th metabolite entering the systemic circulation. This was stated to be: Rate of exit of metabolite from gut wall $[f_a \cdot R_{o,po} \cdot E(d)_g \cdot fm_{i,g}(1 - E(m_i)_g)]$, plus Rate of formation of metabolite from drug entering liver from gut, $[f_a \cdot R_{o,po} \cdot (1 - E(d)_g) \cdot fm_{i,H}]$, both times the fraction of metabolite escaping the liver, $1 - E(m_i)_H$. The term omitted was the rate of systemic metabolite appearance derived from recirculating drug, $[f_a \cdot R_{o,po} \cdot (1 - E(d)_g) \cdot (1 - fe(d) \cdot F_H) \cdot fm_{i,H} \cdot (1 - E(m_i)_H)]$.

The net effect of this correction is to replace $(1 - E(m)_H)$ by $[(1 - E(m)_H) \cdot (1 - fe(d) \cdot F_H)]$ associated with oral drug administration in all equations subsequent to Eq. (1) of ref. 1. For example, Eq. (10) of ref. 7 should read

$$\frac{R_{o,iv}}{R_{o,po}} = \sqrt[n]{\left(\frac{F_H^n + \left\{ \frac{(1 - E(m))(1 - fe(d) \cdot F_H)}{\phi \rho} \right\}^n}{1 + \left\{ \frac{(1 - E(m))(1 - fe(d))}{\phi \rho} \right\}^n} \right)} \quad (3)$$

Despite the error in Eq. (7) of Rowland (1), the simulations performed in the paper are correct. This arises because the simulations dealt with the simplified case of $fe(d) = 0$. Under this circumstance, for example, Eq. (3) above reduces to Eq. (10) of ref. 1.

REFERENCE

1. Rowland, M. Bioavailability assessment and pharmacologic response: Impact of first-pass loss when both drug and metabolites are active. *J. Pharmacokin. Biopharm.* **16**:573-593 (1988).