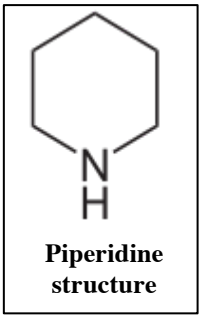
Remifentanil: Pharmacokinetics

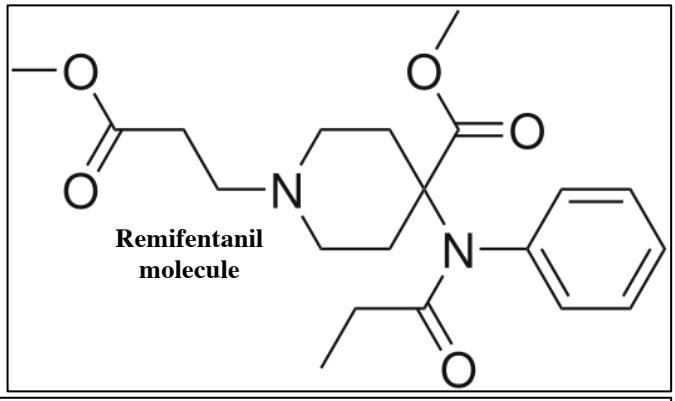
Anesthetic Pearls: The Pharmacokinetics of Remifentanil



Piperidine structure

Remifentanil (marketed by GlaxoSmithKline & Abbott as **Ultiva**) is a piperidine derivative, with methyl-ester linkage. Once reconstituted, it has a pH of +/- 3.0. The reconstituted drug undergoes spontaneous degradation at a pH > 4, but at a pH < 4 it remains stable for approximately 24 hours. Remifentanil has strong affinity for the opioid *mu*, *sigma*, and *kappa* receptors. The potency of remifentanil is about 2 times more than fentanyl and 200 times greater than morphine.

The major metabolite of remifentanil is remifentanil acid which similarly binds to *mu*, *sigma*, and *kappa* receptors but with much lower affinity. The potency of this metabolite is 800-2000 times less than the parent remifentanil compound.



Remifentanil molecule

Remifentanil contains a methyl-ester linkage that makes it susceptible to metabolism by nonspecific esterases in blood and other tissues. The ester hydrolysis breakdown is unchanged by inhibition of plasmacholinesterase or by states of altered plasmacholinesterase function. Remifentanil demonstrates rapid onset, small volume of distribution, rapid redistribution, and brisk clearance with a terminal elimination half-life of 8 – 20 minutes.

Table 1. Pharmacokinetics of Remifentanil Compared with Alfentanil and Fentanyl

	Alfentanil	Fentanyl	Remifentanil
V_1 (L/kg)	0.1–0.4	0.5–1.0	0.1–0.2
V_{DSS} (L/kg)	0.25–0.75	3–5	0.3–0.4
Cl ($mL \cdot min^{-1} \cdot kg^{-1}$)	3–8	10–20	40–60
$t_{1/2}\beta$ (min)	60–120	180–300	8–20
$t_{1/2}$ k_{e0} (min)	0.6–1.2	4–5	1.0–1.5

See References 4–6.
V_1 = volume of distribution of the central compartment, V_{DSS} = volume of distribution at steady-state, Cl = clearance, $t_{1/2}$ β = elimination half-life, $t_{1/2}$ k_{e0} = half-life for equilibration between plasma and its effect compartment.

The context-sensitive half-time is derived from computer simulations that determine the time taken for the plasma drug concentration to decrease by 50% after an infusion. Such simulations also predict that the time for its concentration to decrease by 80% is <15 min for any length of infusion.

The esterase-based metabolism of remifentanil makes it pharmacokinetics independent of end-organ failure. In the elderly, data indicate that the onset of drug effect is slowed and that they are therefore more sensitive to remifentanil.