Because Esmolol (Esm) contains an ester, it is extensively metabolized in blood by esterase and therefore used as an ultra-short acting β-blocker. Cardioselective Esm has been used in the treatment of critically ill patients, and combined with anesthetic drugs during surgery. In this study, the effects of sevoflurane (Sevo) and propofol (Prop) on the kinetics of Esm in dog blood were examined in vivo and in vitro. For the pharmacokinetics (PK) study, Esm (10mg/kg) was administered intravenously to anesthetized (ca 2% Sevo inhalation or 20mg/kg/hr Prop infusion) and conscious dogs. The post-administration changes in Esm concentrations in dog blood were measured. Effects of Sevo and Prop on Esm hydrolysis were examined in an enzyme reaction study. Esm (10 μg/mL) in dog blood containing Sevo (360, 720 μM) or Prop (10, 50 μg/mL) was sequentially incubated at 37°C. In the PK study, the mean of Esm blood concentration-time profiles in the anesthetized dogs was about 2 to 3.5 times higher than that in the conscious dogs, but the half-lives (T1/2) of Esm were almost the same. The area under the Esm blood concentration curve increased about 2 to 2.5 times, and total body clearance and distribution of volume (Vd) decreased to about half in the anesthetized dogs. The enzyme reaction study showed that Esm hydrolysis was inhibited with Prop in a concentration-dependent manner. The T1/2 of Esm was only 10% longer at a clinical concentration of Prop (ca 10 μg/mL), and that of Esm only 30% longer at a clinical concentration of Sevo (ca 720 μM). We believe that the increase in Esm blood concentration was related to the decrease in Vd resulting from the decrease in cardiac output in the anesthetized dogs, rather than that the inhibition of Esm hydrolysis by the anesthetic drugs was the reason for the increase in Esm blood concentration. Esm concentration may thus also increase in human blood during surgery.