**#11_Pharmacological Effects of a New Halogenated Methyl-Ethyl Ether in Rats**

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**Background/Introduction:** We studied a halogenated methyl-ethyl ether (BTTE: 1-bromo-1,1,2-trifluoro-2-(trifluoromethoxy)ethane, CAS: 2356-55-0) to evaluate its potential as an inhaled general anesthetic. We measured partition coefficients, stability in $CO_2$ absorbents, and effects on NMDA and $GABA_A$ receptor currents. In rats, we measured potency to produce immobility in response to noxious stimulation, and bromide and fluoride levels to determine extent of metabolism. For comparison, we also studied groups of rats anesthetized with sevoflurane or halothane.

**Methods:** Saline:gas, oil:gas and blood:gas partition coefficients were determined using headspace techniques (n=4 for each). Stability was evaluated during two-hour exposure at room temperature of BTTE in Amsorb and SodaSorb. Effects of BTTE on NMDA and $GABA_A$ receptor currents were determined using standard techniques in oocytes. Sprague-Dawley rats (N=4) were anesthetized in acrylic cylinders using vaporizers that delivered BTTE. Blood pressure was determined by the tail cuff method. Anesthetic requirements were determined by adjusting the inspired BTTE concentration (measured using gas chromatography), and applying a tail-clamp to elicit gross, purposeful movement. The BTTE concentration was adjusted in an up-and-down method to find the concentrations that permitted, and prevented, movement in response to the clamp; the

minimum alveolar concentration (MAC) was the average of these bracketing concentrations. After 120 minutes of anesthetic exposure, a laparotomy was performed and each rat exsanguinated; bromide and fluoride levels were determined. Two other groups of rats were anesthetized with sevoflurane (N=4) or halothane (N=4) for comparative purposes.

**Results:** The partition coefficients were: S:G = 0.051 ± 0.008; O:G = 31 ± 2; B:G = 0.129 ± 0.013. BTTE was stable in Amsorb, while there was 17.5 ± 0.9% loss in Sodasorb (similar to sevoflurane). At saturated BTTE concentrations, $GABA_A$ currents were enhanced 195 ± 24% (n=5) while NMDA currents (n=6) were unaffected. Anesthetic requirements (MAC) for BTTE were 13.1 ± 0.0%; sevoflurane and halothane requirements were 2.3 ± 0.3% and 1.3 ± 0.1%, respectively. MAP was 91 ± 11 mmHg with BTTE, while it was 76 ± 9 mmHg with sevoflurane and 75 ± 12 mmHg with halothane ($p<0.05$ one-tailed t-test: BTTE vs. sevoflurane and BTTE vs. halothane). After BTTE anesthesia, fluoride concentrations were <LOQ, and bromide ranged from 0.3 ppm to <LOQ. After sevoflurane, fluoride was 0.3 ± 0.0 ppm; after halothane, bromide was 11 ± 5 ppm and fluoride 0.3 ± 0.1 ppm.

**Conclusions**: BTTE appeared to be well tolerated in rats. Receptor data suggest that BTTE acts at $GABA_A$ receptors, but not NMDA receptors. Blood pressure was greater during BTTE anesthesia as compared to those measured during sevoflurane and halothane anesthesia. The fluoride and bromide concentrations were less than those found with sevoflurane and halothane anesthesia, suggesting minimal metabolism. The low B:G partition coefficient suggests that BTTE would have fast kinetics. BTTE shows potential as a new inhalational anesthetic.