Stability of I-653 in Soda Lime

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I-653 is a new, volatile anesthetic that differs from isoflurane by substitution of a fluorine atom for the chlorine found on the α-ethyl component of isoflurane. Thus its formula is CF₂H-O-CFH-CF₃. The substitution of fluorine for chlorine markedly decreases the blood solubility of I-653 from that of isoflurane (blood gas partition coefficients 0.42 vs 1.41, respectively) (1,2), and should also increase stability. A greater stability is desirable; an unstable anesthetic may degrade to toxic compounds in vitro (3-6) and in vivo (7). The following experiment compared the stability of I-653 with the stability of halothane, isoflurane, and sevoflurane in the presence of soda lime at 40, 60, and 80°C.

Methods

Three groups of four and one group (80°C) of five 581-ml flasks were filled with 100 g of fresh soda lime (Sodasorb) containing approximately 15% water by weight. The surface of the soda lime was covered with a Teflon cup to prevent liquid (but not gaseous) anesthetic from reaching the soda lime. Teflon stoppers pierced with needles capped with one-way stopcocks were used to seal the flasks. After air was evacuated from each flask, a liquid mixture of the four anesthetics was added to each. The total liquid volume injected was calculated to produce an initial vapor concentration of 1-3% of each agent. Such concentrations were more than an order of magnitude less than the saturated vapor pressure (i.e., all anesthetic was vaporized). The vapor pressure of I-653 is slightly greater than 700 mm Hg at 23°C (unpublished data). Such vapor concentrations are approximately those used in clinical practice: MAC for sevoflurane in humans is 1.71% (8); that for halothane is 0.75% (9); and that for isoflurane is 1.4% (10). MAC for I-653 in rats is 5.7% (11). Each flask was placed in a waterbath and after 20-30 min, the pressure in each was allowed to reach ambient pressure by the admission of room air. The concentration of each anesthetic was determined by gas chromatography.

For chromatography we used a 30-m, fused silica open tubular capillary column (0.53 mm internal diameter) coated with a layer of methylsilicone oil 1.5-μm thick (J & W Scientific DB-1). A nitrogen carrier stream of 6 ml/min was directed through the column with a “make-up” flow of nitrogen of 40 ml/min delivered to the detector. A flame ionization detector at 200°C was supplied by hydrogen at 40 ml/min and by air at 280 ml/min. Samples were injected with a 0.05-ml gas sample loop.

The first group of four flasks was maintained at 40°C, the second group of four at 60°C, and the last two groups (four and five flasks respectively) at 80°C. The gas in the flasks was serially sampled (sample...
Table 1. Rate of Anesthetic Degradation in Soda Lime (%/hr)

<table>
<thead>
<tr>
<th>Temperature</th>
<th>I-653</th>
<th>Halothane</th>
<th>Isoflurane</th>
<th>Sevoflurane</th>
</tr>
</thead>
<tbody>
<tr>
<td>40°C</td>
<td>0.083 ± 0.086</td>
<td>0.63 ± 0.11</td>
<td>0.20 ± 0.09</td>
<td>12.9 ± 0.4</td>
</tr>
<tr>
<td>60°C</td>
<td>-0.094 ± 0.071</td>
<td>1.56 ± 0.07</td>
<td>0.15 ± 0.06</td>
<td>56.4 ± 4.3</td>
</tr>
<tr>
<td>80°C</td>
<td>0.45 ± 0.26</td>
<td>16.0 ± 1.6</td>
<td>13.1 ± 3.7</td>
<td>92.2 ± 5.2</td>
</tr>
</tbody>
</table>

The rates of degradation reported (mean ± SD) are for the indicated agent placed in a 581-ml flask containing 100 g soda lime. All values for the above rates of degradation differ significantly from zero except for those for I-653 at 40 and 60°C. All values for a given agent differ from the values for the remaining agents at a given temperature. The values for each anesthetic at each temperature are the average from four determinations except for I-653, isoflurane, and halothane at 80°C, where the average for each agent is from five determinations.

Results

Although I-653 did not degrade significantly at 40 or 60°C, it did so at 80°C (Table 1). All the remaining agents degraded at all temperatures (that is, the slope for concentration of anesthetic vs time deviated from zero) (Table 1, Fig. 1). With the exception of the 40–60°C comparison for I-653, for all anesthetics, the rate of degradation increased with each increase in temperature (Table 1, Fig. 2). At all temperatures, the rate of degradation was lowest with I-653 and highest with sevoflurane (Table 1, Figs. 1 and 2). Isoflurane and halothane occupied intermediate positions, with halothane degradation occurring at a faster rate. In all but three comparisons of the average degradation values for each anesthetic, the differences among anesthetics were highly significant (P < 0.001). The differences from each other. For all calculations, differences were considered significant when P < 0.01.
among the three exceptions were less dramatic, but still significant ($P < 0.01$).

Discussion

The results indicate that I-653 is considerably more stable in soda lime than any of the presently used potent volatile anesthetics. At 80°C the stability of I-653 was 29-fold greater than that of isoflurane, the next most stable agent. Such high stability is a desirable property because both in vitro and in vivo breakdown products may be toxic.

The results obtained for halothane, isoflurane, and sevoflurane in the present study are relatively consistent with those previously reported (12). The methods applied in the earlier study were similar to those used in the current experiment except for three conditions: in the previous investigation somewhat lower temperatures were applied; water was added to the soda lime; and regression analyses were performed on grouped data. Despite these differences, the results of both studies are qualitatively similar. There is a small quantitative difference in that the results for the current experiment indicate slightly slower rates of degradation than reported earlier. For example, in the previous study, at 54°C, the rates of degradation for halothane, sevoflurane, and isoflurane were 2.21%/hr, 57.4%/hr, and 0.30%/hr, respectively. In the present study, at 60°C, these rates were 1.56%/hr, 56.4%/hr, and 0.15%/hr, respectively.

References