Volatility of Radiopharmacy-Prepared Sodium Iodide-131 Capsules

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Objective: The aims of this study were to quantify the extent of volatilization from ^{131}I-NaI therapeutic capsules prepared in a centralized radiopharmacy and to quantify the amount of volatile ^{131}I released from a dispensing vial containing a compounded ^{131}I-NaI therapy capsule.

Methods: Therapy capsules were prepared by injecting ^{131}I oral solution into capsules containing anhydrous dibasic sodium phosphate. Volatilized activity was obtained by filtering air drawn across samples that were placed open on the bottom of a sample holder cup. Volatile ^{131}I was captured by filtering it through 3 triethylenediamine-impregnated carbon cartridge filters, arranged in series. To quantify the amount of volatile ^{131}I released from a dispensing vial during a simulated patient administration, a vial containing a compounded ^{131}I therapy capsule was opened inside a collapsible plastic bag and all the air was drawn across TEDA-impregnated carbon cartridge filters.

Results: The 370-MBq (10-mCi) ^{131}I capsules from the first part of the experiment released an average of 0.035% (SD 0.031%) of the capsule activity on the first day, 0.012% (SD 0.002%) on the second day, and 0.012% (SD $<$ 0.001%) for days 3 through 5. The 37-MBq (1-mCi) ^{131}I capsules released an average of 0.058% (SD 0.025%) on the first day, 0.029% (SD 0.009%) on the second day, and 0.020% (SD 0.004%) on the third day. The activity released from the vial during a simulated patient administration was 0.00093% of the ^{131}I capsule activity.

Conclusion: The amount of ^{131}I, which volatilized daily from the exposed therapy capsules, was a small percentage of the capsule activity. The volatile ^{131}I that would be released during a patient administration was much less than the activity that volatilized from the exposed therapy capsules.

Key Words: radioiodine; volatility; radiation safety; radiopharmacy

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Radioiodine has been an essential part of nuclear medicine practice since Saul Hertz, Arthur Roberts and Robley Evans studied thyroid physiology using ^{128}I in 1937 (*1*,*2*). In January 1941, Hertz and Roberts were the first to administer radioiodine ^{131}I for the treatment of hyperthyroid patients (*3*). Today, almost 60 y later, radioiodine therapy with ^{131}I remains the primary therapeutic agent used in nuclear medicine, and its use is firmly established in the 2 diseases first treated: hyperthyroidism and thyroid carcinoma.

Initially the use of ^{131}I was restricted to the only pharmaceutical dosage form then available—liquid oral solution. While liquid radioiodine proved to be beneficial to the patients to whom it was administered, the frequency of contamination and thyroid uptake activity in nuclear medicine personnel who handled the material was noted with increasing alarm (*4–7*). This contamination of and unnecessary exposure to occupational workers prompted the dissemination of a report by the NRC in 1977 advising licensees of the issue (*8*).

In response to these concerns, manufacturers of liquid radioiodine reformulated their products to make them less volatile. This was accomplished by adding sodium bisulfate as an antioxidant, a disodium phosphate buffer to maintain an alkaline pH and disodium edetate (EDTA), a chelating agent to prevent catalytic oxidative reactions induced by metal ions (*9–11*).

Although the volatility of ^{131}I solution has been reduced, there is still the significant risk of spillage and contamination inherent with liquid ^{131}I solution. Encapsulation of ^{131}I has proven to be a highly effective method of decreasing these risks. The routine use of radioiodine capsules has become standard practice in the majority of nuclear medicine departments in North America because of their reduced risk of radioactive contamination due to spills, volatility and ease of patient administration.

Airborne contamination, however, still occurs with capsules (*12–14*) and can be a source of concern for those handling these doses. The aim of this experiment was to determine the amount of volatile ^{131}I released from capsules prepared in a centralized nuclear pharmacy.

This experiment was designed to answer 2 questions. First, what was the daily rate percentage of ^{131}I that volatilized and was released from radiopharmacy-compounded therapy capsules when they were left open and placed on the bottom of the

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sample holder cup over several days. Second, what was the percentage of volatilized ^{131}I released when a dispensing vial containing a radiopharmacy-compounded therapy capsule that had been stored for 24 h was opened during a simulated patient administration.

MATERIALS AND METHODS

Sample Preparation

Each ^{131}I-NaI therapy capsule was compounded as a capsule within a capsule. The inner capsule was prepared by filling a #1 empty gelatin capsule (Shionogi Qualicaps Inc., Whitsett, NC) with anhydrous dibasic sodium phosphate, USP (Spectrum Quality Products, Inc., Gardena, CA). Iodine-131 as sodium iodide oral solution, USP (CIS-US Inc., Bedford, MA), stabilized with 1mg/mL EDTA, USP (Abbott Laboratories, North Chicago, IL), was injected into the inner capsule using a hubless insulin syringe. Capsules containing 37 MBq (1 mCi) and 370 MBq (10 mCi) ^{131}I were prepared by injecting 0.10 ± 0.01 mL ^{131}I-NaI into the capsules. A 481-MBq (13-mCi) capsule was prepared for the simulated patient administration by injecting 0.32 ± 0.01 mL of solution into the capsule. The compounding was completed by placing a #0 gelatin capsule snugly over the inner capsule.

Volatility Determination

Figure 1 shows the experimental configuration used to determine the extent of volatilization from ^{131}I therapeutic capsules. Individual capsules were placed open on the bottom of the sample holder cup. A vacuum-driven filter cartridge system was fitted into the sample holder cup and used to trap volatilized ^{131}I escaping from the ^{131}I therapy capsule. Filter cartridges containing activated charcoal impregnated with 5% triethylenediamine (TEDA), a chelating agent used to chemically bind the iodine and reduce loss by desorption, were used (Hi-Q Environmental Products Co., San Diego, CA). These cartridges are certified by the manufacturer to be 99% efficient for trapping methyl iodine at airflow below 10 L/min. These

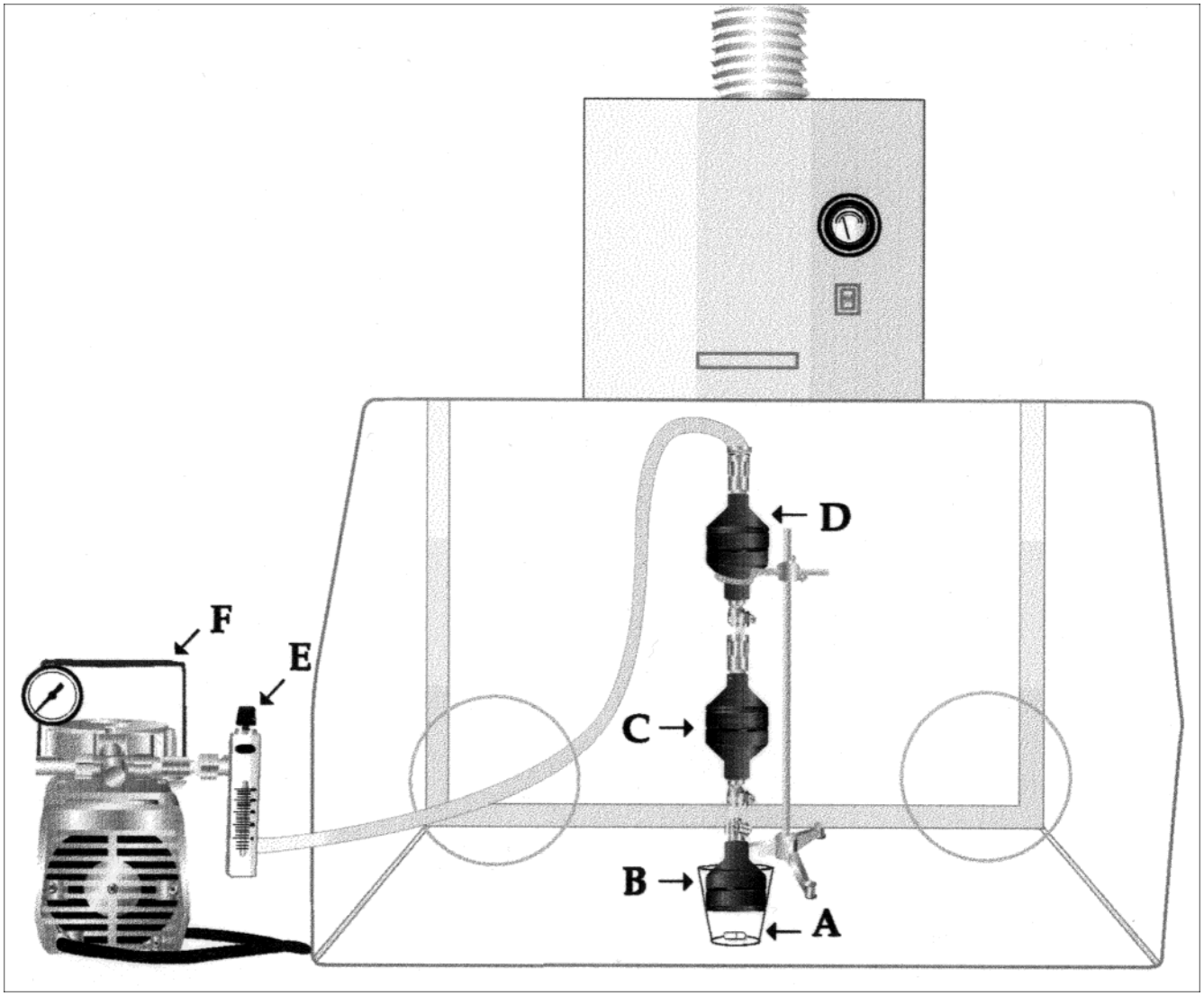

FIGURE 1. Schematic diagram of the apparatus used to measure the volatility of ^{131}I therapy capsules with (A) sample holder, charcoal filter holders (B) F-1, (C) F-2 and (D) F-3. Negative airflow was maintained with a (F) vaccum pump and (E) flowmeter.

filters were arranged in series with Teflon tubing and numbered F1 through F3, with F1 being closest to the sample. Before use, a visual $C0_2$ vapor (dry ice) test was performed on the apparatus to ensure that air was being drawn into the sample holder cup and then up through the filter arrangement. An airflow rate of 5 L/min was pulled through the 0.2-cm gap between the filter holder and sample holder cup, then up through the filter cartridges in series. The filters were replaced daily and the removed filters were measured for radioactivity immediately after their removal.

In the simulated patient administration portion of the experiment, the ^{131}I capsule was stored in a plastic 3-dram snap-cap vial (VWR Scientific Products, S. Plainfield, NJ) for 24 h. The vial then was placed into a 2-L plastic bag that had its opening secured around the sides of the first filter holder. The vial was opened and the filter system was activated until the bag was fully collapsed. A hole was punctured in the far end of the bag and the filter system was allowed to pull air through the bag for 5 min. The system was shut down and the filters were removed and immediately measured for radioactivity.

A single-channel analyzer (SCA) was used to measure the radioactivity deposited on the filters used in both parts of this experiment. Two-minute counting rate values were converted to counts per minute (CPM) and corrected for SCA deadtime. Because 0.6% of the decay of ^{131}I results in a daughter product ^{131m}Xe with a 164-keV photopeak, a 364-keV photopeak iodine-specific window was used for counting the charcoal filters (*15*). An efficiency factor, obtained using a 300–430-keV SCA window and a calibrated, NIST traceable ^{133}Ba disk source of geometry identical to that of the filter cartridges (Isotope Products Laboratory, Burbank, CA), was used to convert counts per minute (CPM) to disintegrations per minute (DPM) (CPM × Efficiency factor = DPM). The filter DPM was converted to MBq and adjusted to the midpoint of the 24-h sample period using a 12-h decay factor. The time-adjusted MBq activities for F1 through F3 were summed and normalized against the capsule activity decayed to the same point in time. This resulted in daily values for the percent of capsule activity deposited on the filters.

In addition, glovebox filter monitoring, glovebox surface wipe tests and F3 filter count values of background were evidence that volatile ^{131}I was not escaping filter entrapment. Wipe tests of the inner surface of the sample holder in part one of the experiment, and the collapsible bag in part two of the experiment, detected no adsorption of ^{131}I onto these surfaces.

RESULTS

Tables 1 and 2 show the percentages of activity from the 370-MBq (10-mCi) and 37-MBq (1-mCi) ^{131}I therapy capsules that were deposited in the filters in the first part of the experiment. The average percentage of all the activity that volatilized from the 370-MBq (10-mCi) ^{131}I capsules for Day 1 was 0.035% (SD 0.031%), for Day 2 was 0.012% (SD 0.002%), and for Days 3 through 5 was 0.012% (SD < 0.001%). The average percentage of all activity that volatilized from the 37-MBq (1-mCi) ^{131}I capsules for Day 1 was 0.058% (SD 0.025%), for Day 2 was 0.029% (SD 0.009%), and for Day 3 was 0.020% (SD 0.004%).

TABLE 1
Percentage of Capsule Activity on Filters for 370-MBq (10-mCi) Iodine-131 Capsule Trials

		% Capsule activity on filter		
Trial	Day	F1	F2	F3
1	1	1.30^{-02}	5.60^{-06}	$<1.0^{-07}$
	2	1.10^{-02}	7.60^{-05}	$<1.0^{-07}$
	3	1.30^{-02}	4.00^{-07}	$<1.0^{-07}$
	4	1.20^{-02}	4.40^{-06}	$<1.0^{-07}$
	5	1.20^{-02}	6.40^{-06}	$<1.0^{-07}$
2	1	5.70^{-02}	1.00^{-05}	$<1.0^{-07}$
	2	1.40^{-02}	3.60^{-06}	$<1.0^{-07}$
	3	1.20^{-02}	1.50^{-05}	$<1.0^{-07}$
	4	1.20^{-02}	4.30^{-07}	$<1.0^{-07}$
	5	1.20^{-02}	1.50^{-05}	$<1.0^{-07}$

In the simulated patient administration of a 481-MBq (13-mCi) ^{131}I therapy 4.07 Bq capsule (0.11 μCi) escaped from the dispensing vial when it was opened after 24 h of storage. This was 0.00093% of the dose activity.

CONCLUSION

The amount of ^{131}I that volatilizes from radiopharmacy compounded sodium iodide therapy capsules is minimal. Only a small percentage of the activity present in the capsules is released as volatile.

The amount of volatile ^{131}I released during a patient dose administration is expected to be considerably less than that indicated by the data obtained here from an ^{131}I therapy capsule left open and exposed. During patient dose administration, the amount of volatile ^{131}I released would be on the order of 0.001% of the dose activity. These results support the belief that radiopharmacy-compounded ^{131}I therapy capsules are safe and convenient for both the patient and nuclear medicine personnel.

TABLE 2
Percentage of Capsule Activity on Filters for 37-MBq (1-mCi) Iodine-131 Capsule Trials

		% Capsule activity on filter		
Trial	Day	F1	F2	F3
1	1	7.30^{-02}	9.80^{-05}	$<1.0^{-07}$
	2	3.40^{-02}	1.10^{-04}	$<1.0^{-07}$
	3	2.20^{-02}	7.60^{-05}	$<1.0^{-07}$
2	1	4.70^{-02}	1.70^{-05}	$<1.0^{-07}$
	2	1.60^{-02}	1.80^{-05}	$<1.0^{-07}$
	3	1.70^{-02}	3.00^{-05}	$<1.0^{-07}$
3	1	8.40^{-02}	4.40^{-05}	$<1.0^{-07}$
	2	2.90^{-02}	5.20^{-05}	$<1.0^{-07}$
	3	2.30^{-02}	3.10^{-05}	$<1.0^{-07}$
4	1	2.90^{-02}	9.30^{-06}	$<1.0^{-07}$
	2	3.60^{-02}	7.20^{-06}	$<1.0^{-07}$
	3	1.60^{-02}	1.30^{-05}	$<1.0^{-07}$

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REFERENCES

1. Hertz S, Roberts A, Evans RD. Radioactive iodine as an indicator in the study of thyroid physiology. *Proc Soc Exp Biol Med.* 1938;38:510–513.
2. Hamilton JG. The rates of absorption of the radioactive isotopes of sodium, potassium, chlorine, bromine and iodine in normal human subjects. *Am J Physiol.* 1938;124:667–678.
3. Hertz S, Roberts A. Application of radioactive iodine in therapy of Graves' disease [Abstract]. *J Clin Invest.* 1942;21:624.
4. Howard BY. Safe handling of radioiodinated solutions. *J Nucl Med Technol.* 1976;4:28–30.
5. Browning EJ, Banerjee K, Reisinger W. Airborne concentration of I-131 in a nuclear medicine laboratory. *J Nucl Med.* 1978;19:1078–1081.
6. Goble JC, Wagner WM. Volatilization during iodine therapies: assessing the hazard [Abstract]. *Health Physics*. 1978;35:911.
7. Jackson GL, MacIntyre F. Accumulation of radioiodine in staff members [Letter]. *J Nucl Med.* 1979;20:995.
8. Singer B. Letter to all medical licensees concerning radioactive iodine volatility from sodium iodide oral solutions. Washington, DC: US Nuclear Regulatory Commission; 1977.
9. Wolfangel R. Accumulation of radioiodine in staff members [Reply to Letter]. *J Nucl Med.* 1979;20:995.
10. Murphy P. Letter to radioiodine customers announcing sodium iodide oral solution reformulation. St. Louis, MO: Mallinckrodt, Inc.; April 2, 1979.
11. Luckett LW, Stotler RE. Radioiodine volatilization from reformulated sodium iodide I-131 oral solution. *J Nucl Med.* 1980;21:477–479.
12. Shearer DR, Donovan GL, Moore MM. Contamination from therapeutic ^{131}I capsules. *Health Phys.* 1985;49:81–83.
13. Hackett MT, Perdikaris N, Ruffin TT. Additional radiation safety concerns involving sodium iodide-131 capsules. *J Nucl Med Technol.* 1995;23:289–290.
14. Ficken VJ. Additional radiation safety concerns involving sodium iodide-131 capsules [Letter]. *J Nucl Med Technol.* 1996;24:139.