
Influence of Iodine-131 Solution Volume and Storage Time on In Vitro Dissolution

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Objective: This investigation was conducted to determine the influence of ^{131}I solution volume and storage time on the in vitro release of radioiodide from capsules.

Methods: In vitro dissolution profiles for ^{131}I sodium iodide capsules compounded in a centralized nuclear pharmacy were determined using the USP XXIII Dissolution Test. Iodine-131 solution volumes of 0.05, 0.15 and 0.25 ml and storage times of 2, 5, 7 and 9 days were considered.

Results: By 80 min after initiation of the dissolution test, more than 95% of the ^{131}I was released from capsules prepared with 0.15 and 0.25 ml of the ^{131}I solution. The 0.05-ml capsules reached 95% at 55 min. Capsules prepared with 0.05 ml of solution and stored 2, 5, 7 or 9 days released over 95% of the radioactivity within 65 min. Capsules prepared with 0.25 ml of solution and stored for 2, 5, 7 or 9 days released over 95% of the ^{131}I by 55 min after initiation of the dissolution test.

Conclusion: Neither the different volume of radioactive sodium iodide solution used in the preparation of capsules nor the time of storage greatly influenced the release of ^{131}I from the capsules. Based on dissolution profiles, it appears that the bioavailability of ^{131}I would not be influenced by factors studied in this investigation.

Key Words: iodine-131; solution volume; storage time; compounded capsules; centralized nuclear pharmacy

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Iodine-131 sodium iodide capsules are compounded in a centralized nuclear pharmacy to meet the specific needs of each patient. A common method involves the filling of a gelatin capsule with a diluent followed by injection of a small volume of radioactive sodium iodide solution into the intact capsules. This is followed by encapsulation with a size larger gelatin capsule.

The volume of radioiodide solution will vary depending on the amount of activity required. Capsules may be prepared in

anticipation of need and retained for a specific expiration time. The influence of radioiodide solution volume used to prepare capsules and the time of storage on the release of radioactive iodide has not been investigated. If these variables do influence radioiodide release characteristics, the potential exists for variations in the bioavailability of radioiodide for uptake by the thyroid.

The USP XXIII Dissolution Test was used in this investigation (1) to determine dissolution profiles for sodium iodide capsules prepared with different radioiodide solution volumes and stored for varying time periods before dissolution studies. While not official for ^{131}I sodium iodide capsules, the USP Dissolution Test has been shown to be useful in detecting the influence of formulation and lubricant on in vitro dissolution for ^{131}I sodium iodide capsules (2). Also, in vitro dissolution profiles have been determined for commercially available diagnostic (3) radioiodide capsules as well as capsules for therapy (4).

MATERIALS AND METHODS

Compounded Capsules

The ^{131}I sodium iodide capsules used in the investigation were prepared by a centralized nuclear pharmacy (Radiopharmacy Inc., Evansville, IN). The methodology used in the routine provision of sodium iodide capsules to commercial customers was used in preparing the ^{131}I capsules for the dissolution study. Sodium iodide capsules were prepared by filling number one capsules with sodium phosphate dibasic powder. The appropriate volume of ^{131}I solution was injected followed by encapsulation with a number zero capsule. Radioiodide capsules were prepared and shipped to be received for study 1 day after preparation. The radioactivity contained in the compounded capsules ranged from 7.6 to 8.6 μCi .

Experimental Design

Four capsules were prepared each with 0.05 ml, 0.15 ml or 0.25 ml of ^{131}I sodium iodide solution from the same lot. Dissolution profiles were determined for the four capsules with each volume of ^{131}I sodium iodide solution to ascertain the

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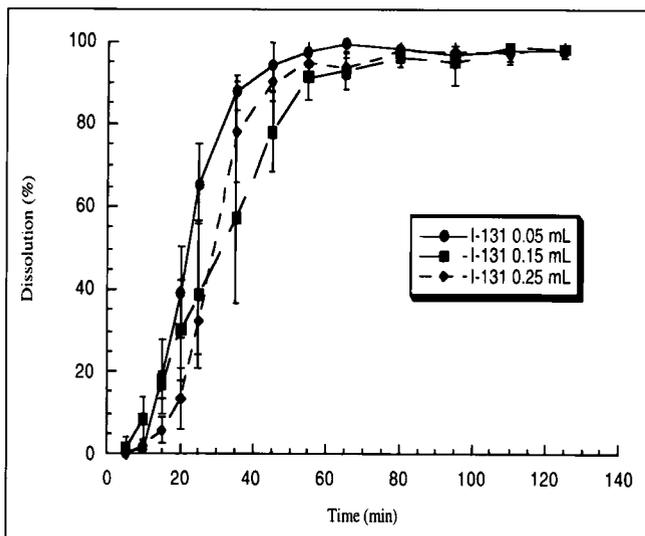


FIGURE 1 The influence of radiiodide sodium iodide solution volume on dissolution profiles (four capsules per volume).

influence of solution volume. The influence of storage time was determined using capsules prepared with either 0.05 ml or 0.25 ml ^{131}I sodium iodide solution from the same lot. Four capsules for each volume were studied at 2, 5, 7 and 9 days after preparation.

Dissolution Test

Dissolution studies were conducted according to the USP XXIII Dissolution Test method (1). Briefly, each unit consisted of a 1000-ml glass beaker and a motor-driven metallic shaft connected to a paddle blade. The stirring element was placed at the prescribed distance of 25 ± 2 mm from the bottom of the 1000-ml glass beaker and rotated at 50 rpm. Each beaker contained 900 ml distilled water maintained at $37 \pm 0.5^\circ\text{C}$. Sampling (1 ml) was conducted at 5, 10, 15, 20, 30, 40, 50, 65, 80, 95, 110, 125 and 140 min after placing the capsules in the beaker. Each capsule was placed in a wire cage to prevent floating. A volume of distilled water equal to the sample was added to each beaker immediately after each sampling. Using the methodology of Yu (3), the samples were counted in an autogamma counter (Minaxi 5000[®]; Packard Inc., Meriden, CT). An aliquot of an ^{131}I solution used to prepare capsules also was counted to determine the activity level in each capsule. Net sample counts were corrected for background, counting efficiency, radioactive decay and volume factor. Data were expressed as a percentage of initial activity.

RESULTS

Volume Factor

As noted in Figure 1, the use of 0.05 ml, 0.15 ml or 0.25 ml ^{131}I sodium iodide solution to prepare capsules did not drastically affect the release of the ^{131}I in vitro. By 80 min, 95% or greater of the activity was released from capsules prepared with 0.15 ml and 0.25 ml of solution while capsules prepared with 0.05 ml reached 95% at 55 min. By 80 min, the release of ^{131}I was basically the same for all three volumes. An ANOVA

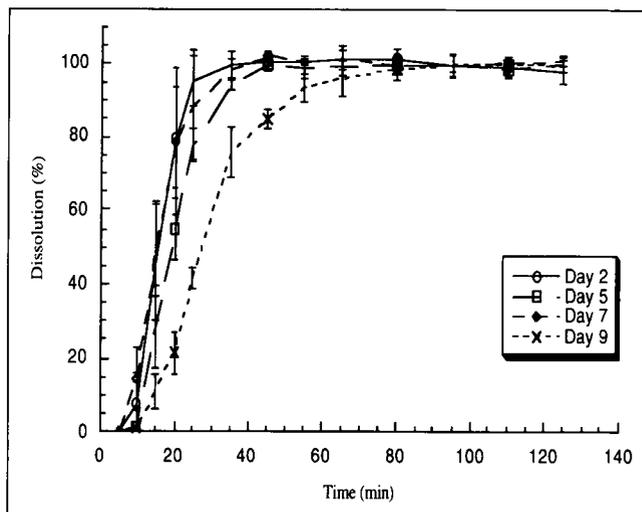


FIGURE 2 The influence of storage time on dissolution profiles (0.05 ml ^{131}I solution, four capsules per storage time).

comparison of the overall release patterns between the three volumes indicated there was no statistical difference from 0–125 min in the dissolution profiles ($p > 0.05$). Comparing the release pattern from 0–35 min, did not show any statistical difference either ($p > 0.05$). As noted in Figure 1, the standard deviations are larger at early sampling intervals and much smaller later. The large variations may be due to an inadequate stirring capacity of the dissolution apparatus during a period of rapid release. This is a normal finding and typical of the outcome using the USP apparatus for dissolution test. After equilibrium, the standard deviations are small. The small deviations may be attributed to no further release of ^{131}I at 95 min after initiating the experiment.

Storage Time

Figures 2 and 3 provide outcome data for capsules studied at 2, 5, 7 and 9 days after preparation. As seen from the data in

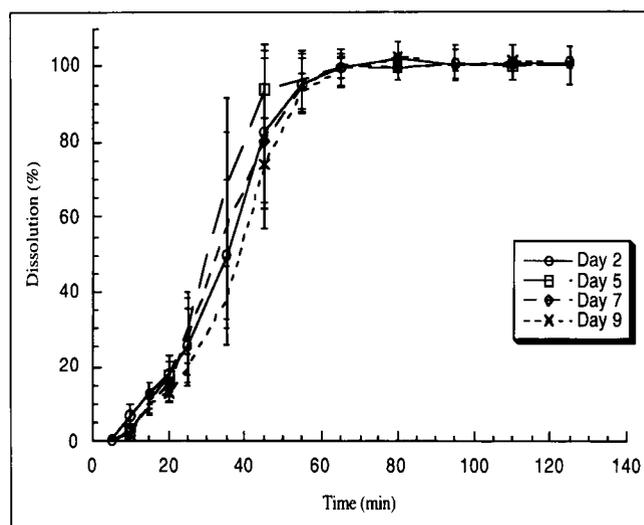


FIGURE 3 The influence of storage time on dissolution profiles (0.25 ml ^{131}I solution, four capsules per storage time).

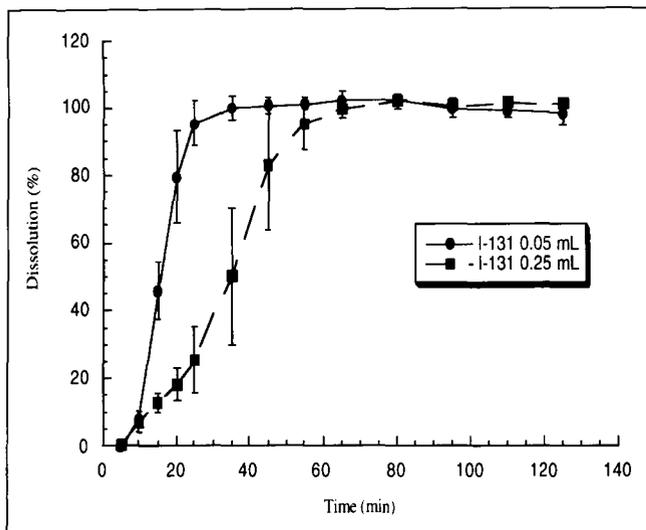


FIGURE 4 The influence of storage time on dissolution profiles (Day 2, four capsules per volume).

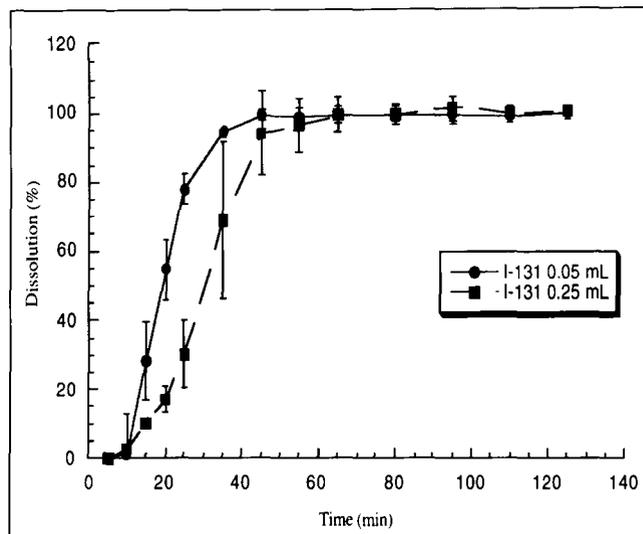


FIGURE 5 The influence of storage time on dissolution profiles (Day 5, four capsules per volume).

Figure 2, storage time resulted in some differences in the release of ^{131}I from capsules prepared with 0.05 ml solution. Perhaps the most significant difference in release patterns was the slower release of radioactivity over the first 65 min from capsules stored for 9 days. Capsules stored 2, 5 or 7 days released over 95% at 45 min after initiation of the dissolution study while capsules stored for 9 days did not release over 95% until 65 min after initiation of the study.

According to the ANOVA test ($p > 0.05$), storage time did not influence overall release patterns from capsules prepared with 0.05 ml solution. Moreover, comparing the release patterns only from 0–20 min did not result in a statistical difference either ($p > 0.05$). There does not appear to be a serious difference in the dissolution profiles for capsules prepared with 0.05 ml radioiodide solution when stored over the time intervals studied in this investigation.

Figure 3 provides dissolution data for capsules prepared with 0.25 ml ^{131}I sodium iodide solution and studied at 2, 5, 7 and 9 days after preparation. On average 95% release of ^{131}I occurred within 55 min. Using the ANOVA statistical test, no statistical differences were found between dissolution profiles for 0.25-ml capsules stored for 2, 5, 7 or 9 days. Furthermore, there was no statistical difference when comparing release patterns from 0–35 min.

As noted in Figure 2 as compared to Figure 3, the release pattern at early sampling intervals for capsules prepared with 0.25 ml solution appears slower than for capsules prepared with 0.05 ml. Figures 4 through 7 compare the influence of storage time on dissolution profiles for capsules prepared with 0.05 ml versus 0.25 ml ^{131}I sodium iodide solution at each day of storage. The Student's t-test indicated that the release patterns during 0–25 min between capsules prepared with 0.05 ml and 0.25 ml were statistically different only on Day 2 of storage ($p < 0.05$) and Day 7 of storage ($p < 0.05$). However, the true significance biologically of about a 30-min difference in attaining over 95% release of ^{131}I in vitro is not known, but likely to be insignificant.

DISCUSSION

Radioiodide sodium iodide capsules are used commonly to aid in assessing thyroid disease and in treating thyroid disorders. Assurance of the bioavailability of the radioiodide for uptake by the thyroid is essential for obtaining the desired outcome. Variability in the bioavailability of radioiodide between dosage forms or products from different vendors could affect the outcome of a diagnostic radioactive iodide uptake study and the subsequent treatment of a condition such as hyperthyroidism. Dissimilarities in ^{131}I release rates between diagnostic and therapeutic capsules could lead to excessive or inadequate therapeutic doses of ^{131}I . If a diagnostic capsule exhibits a poor release rate, the percentage uptake value may be reduced, yet still indicate a hyperthyroid state. Subsequent treatment with a therapy capsule exhibiting a high release rate

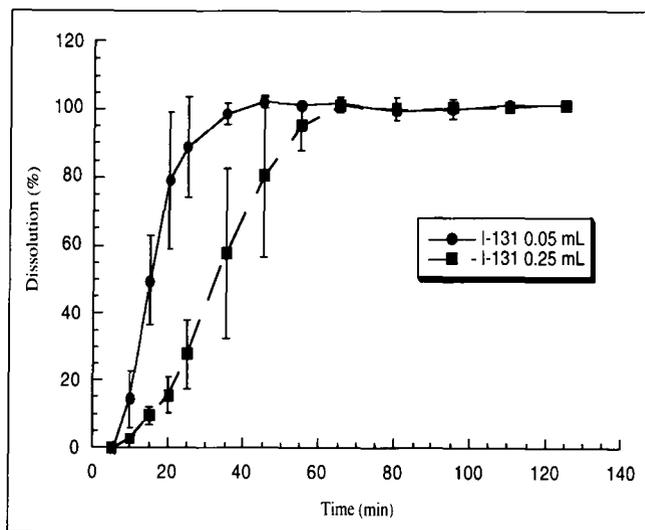


FIGURE 6 The influence of storage time on dissolution profiles (Day 7, four capsules per volume).

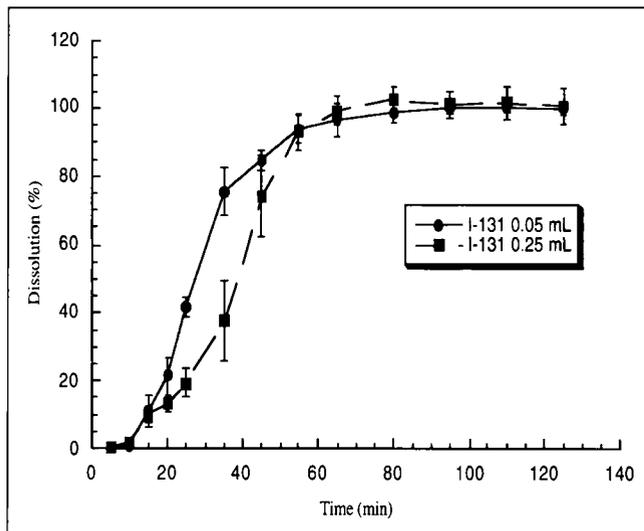


FIGURE 7 The influence of storage time on dissolution profiles (Day 9, four capsules per volume).

could result in excessive radiation dose to the thyroid as the dose of radioiodide would be based on an incorrect lower percentage value.

In our laboratories the USP Dissolution Test has been used to study the *in vitro* radioiodide release profiles for radioiodide sodium iodide capsules. Although the test is not official for radioiodide sodium iodide capsules, it is an official test for therapeutic drugs contained in capsules or tablets. The USP Dissolution Test would appear just as applicable to sodium iodide capsules and should provide useful information regarding the rate of release of radioiodide and, thus, the potential bioavailability *in vivo*. In an investigation of ^{131}I sodium iodide diagnostic capsules, differences in *in vitro* ^{131}I dissolution profiles were noted in the product from one commercial vendor compared to two others (3). The time to attain 100% release was 15–35 min for capsules from two vendors while the release of ^{131}I from a third vendor was slow and reached only 85% after 240 min of study. In contrast, therapeutic ^{131}I sodium iodide capsules from the same vendors all exhibited a rapid release of ^{131}I when subjected to the USP Dissolution Test (4). Almost 100% of ^{131}I release was attained over a period of 15–35 min. Further studies (2), using in-house prepared radioiodide sodium iodide capsules, demonstrated the influence of formulation and lubricant used to prepare granulations for filling sodium iodide capsules. Excellent to poor *in vitro* release of ^{131}I was attained depending on the constituents and lubricant used.

In the current investigation, the dissolution profiles obtained for the compounded ^{131}I sodium iodide capsules were similar

to those found for commercially available sodium iodide capsules. The compounded capsules prepared with different volumes of ^{131}I sodium iodide solution and/or stored for several days released over 95% of the ^{131}I over a time period of 55–80 min. While it is not possible to directly compare the commercial products with the compounded capsules, because of the unknown parameters in preparing commercially prepared products, the dissolution patterns are reasonably close. Thus, it would appear that the bioavailability of ^{131}I between the products would be similar.

CONCLUSION

The dissolution profiles generated for capsules prepared by the centralized nuclear pharmacy were not particularly different from those obtained from previous studies of commercially available diagnostic and therapeutic capsules. The volume of ^{131}I sodium iodide solution used to prepare the capsules investigated in this study did not significantly change the dissolution profiles. For a given volume, storage time up to 9 days did not appear to produce a drastic difference in dissolution profiles. The early release rate differed between 0.05-ml and 0.25-ml capsules at certain days after storage, while differences were minimal at other days. However, large differences in dissolution patterns were not noted. For the most part variations in preparation volumes and storage times studied in this investigation did not result in significantly different dissolution profiles for the ^{131}I sodium iodide capsules.

The USP XXIII Dissolution Test is not official for sodium radioiodide capsules nor have *in vitro* dissolution profiles been related to radioiodide thyroid uptake in humans. Thus, the evidence presented by the *in vitro* dissolution studies conducted in this investigation cannot be unequivocally equated to expected outcomes in the human. Further work relating *in vitro* dissolution patterns to radioiodide uptake in the thyroids of animals would be useful.

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