FIG. 1. Histogram of hypoglycemic effect of insulin (1 u/kg B.W. 1 hr after s.c. administration).

FIG. 2. Histogram of hypoglycemic effect of Zea styles (2 g/kg B.W. 3 hr after s.c. administration).

FIG. 3. Combined histogram of hypoglycemic effect of: *A*—Zea styles (2 g/kg B.W. 3 hr after s.c. administration) and *B*—Insulin (1 u/kg B.W. 1 hr after s.c. administration).

FIG. 4. Hypoglycemic effect of repeated s.c. administration of Zea styles decoction (2 g/kg B.W. in terms of dried drug).

Summary. Macerated decoction extracts of Zea styles exert consistent hypoglycemic effects in fasting rabbits provided they are administered parenterally. Repeated daily subcutaneous administration of the extract to non-fasting rabbits produces even fatal hypoglycemia. The statistical pattern of the hypoglycemic effect of Zea styles compares well with that of crystalline insulin and the distribution is of the gaussian normal curve. The concomitant toxic effects of the hypoglycemic extract, especially when administered intravenously, cannot be accounted for by its blood sugar reducing principle since we could separate the toxic effect from the blood sugar reducing effect.

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1. Pharmacopoea Helvetica, Bern 1953 (German ed.), p. 993.

2. Lewis, J. J., *Physiol. Rev.,* 1949, v29, 75.

3. Peters, G., *Dtsch. Med. Wchschr.,* 1957, v82, 320.

4. Goldner, M. G., *A.M.A. Arch. Int. Med.,* 1958, v102, 820.

5. Farkas, P., personal communication.

6. Gnadt, A. F., *Pharmazie,* 1946, v1, 103.

7. Mirsky, I. A., Diengott, D., Perisutti, G., *Endocrinology,* 1956, v59, 715.

8. Haagen-Smit, A. J., Dandluker, W. B., Wittwer, S. H., Murneek, A. E., *Am. J. Botany,* 1946, v33, 118.

9. Rappaport, F., Eichhorn, E., *Am. J. Clin. Pathol.,* 1950, v20, 834.

10. Dixon, W. J., Massey, F. J., *Introduction to statistical analysis,* McGraw-Hill Book Co., Inc., 2nd ed., 1957, p. 381.

11. Diengott, D., personal communication.

12. Rademaker, C. J., Fisher, J. L., *Am. J. Pharmacy,* 1886, v58, 369.

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Uptake of I^{131} by Rat Organs and Body Fluids Following Injection of Different I^{131} Preparations.* (27460)

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Filter paper chromatography of aged solutions of NaI^{131}(1) or of some samples of commercially available NaI^{131}(2,3) show the presence of non-iodide I^{131} component which moves slightly faster than the NaI^{131} band. This compound has been described as "extraneous" I^{131}(1,4,5) or as component "S"(2) or as "U"(3). It is now well established that this compound has chemical and biological properties which are different from that of NaI^{131}(1,2,3,4) and that its presence in radioautograms of radioiodide solutions cannot be caused by chromatographic artifacts(6).

The present report concerns the rate of uptake of NaI^{131} or of "extraneous" I^{131} by rat organs and body fluids following intraperitoneal injection of one microcurie of each compound.

Methods. Isolation of "extraneous" I^{131} and NaI^{131}. Several microcuries of cysteine-free radioiodide solutions (furnished by E.

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R. Squibb and Sons, New Brunswick, N. J.) were spotted on sheets of filter paper and one dimensionally developed in an ascending technic using n-butanol saturated with 3N NH_4OH(1). After 20 hours, the papers were air-dried and radioautographed. The "extraneous" I^{131}, which moves slightly faster than NaI^{131} and the NaI^{131} band, were cut out and eluted with 50% alcohol. The eluates were evaporated under nitrogen to a concentration of 5 μc/ml.

Uptake studies on rats. Adult female rats of the Holtzman strain weighing between 250-260 g were placed individually in glass beakers with specially designed wire mesh bottoms. Rats were given no food or water during the experiment. Four animals in each group were injected intraperitoneally with 1 μc of either "extraneous" I^{131} or NaI^{131}. At the end of 1, 3 and 24 hours the animals were killed and the radioactivities in various organs and body fluids were determined by the use of a well counter.

Chromatography and radioautography of rat urine. One-hour urine samples from rats injected with NaI^{131} or "extraneous" I^{131} were spotted in 50 microliter amounts on Whatman No. 1 filter paper strips and one dimensionally developed in an ascending technic using n-butanol saturated with 3N NH_4OH. After 20 hours, the papers were air-dried and radioautographed. The "extraneous" I^{131} and the NaI^{131} bands were cut out, eluted with 50% alcohol and counted in a well counter.

Results. The results on rate of uptake of injected NaI^{131} or "extraneous" I^{131} by the thyroid gland are plotted in Fig. 1. At 1, 3, and 24 hours after injection the uptake of NaI^{131} or "extraneous" I^{131} by the thyroid gland increases rapidly with time showing an increased entry of the labeled iodine into the gland and a remarkable retention of the isotope. Also, at 1, 3, or 24 hours following injection the uptake of NaI^{131} by the thyroid gland is significantly higher than that of "extraneous" I^{131}.

The results on rate of uptake of NaI^{131} or "extraneous" I^{131} by the liver, intestine and stomach (Fig. 2, 3, 4) show a faster uptake and removal of I^{131} in comparison to that of the thyroid gland. At 1 and 3 hours after injection, the uptake of NaI^{131} was significantly higher in all the 3 organs when compared to the uptake of the "extraneous" I^{131}. However, at 24 hours following injection, there is a marked lowering of the uptake of NaI^{131} or "extraneous" I^{131} and there are no significant differences in the uptake of NaI^{131} or "extraneous" I^{131} by these organs. Studies on rate of uptake of NaI^{131} or "extraneous" I^{131} by heart, kidney, lung, spleen, pancreas and adrenal glands at 1, 3 and 24 hours showed less than 1% uptake of NaI^{131} or "extraneous" I^{131} and there were no significant differences in uptake of NaI^{131} or "extraneous" I^{131}.

The results of the rate of uptake of NaI^{131} or "extraneous" I^{131} by plasma are plotted in Fig. 5. There is a rapid increase in uptake of NaI^{131} and "extraneous" I^{311} up to 3 hours following injection. However, there is a gradual decline in uptake of the labeled iodine between 3 and 24 hours following injection. At 1 hour and 3 hours after injection, the uptake of NaI^{131} by plasma is significantly higher than that of "extraneous" I^{131}.

The results on rate of urinary excretion of NaI^{131} or "extraneous" I^{131} are shown in Fig. 6. There is a rapid increase in excretion of NaI^{131} or "extraneous" I^{131} during the first 3 hours, which gradually levels off at 24 hours. No significant differences were observed in the amounts of the isotope excreted in the urine. The results on the radioautography of one-hour urine samples from rats receiving "extraneous" I^{131} indicate that 50% of the radioactivity excreted is still present as "extraneous" I^{131} (Fig. 7). However, the data on the radioautography of one-hour urine samples from rats receiving NaI^{131} indicate that 90% of the total radioactivity excreted in the urine is present as NaI^{131} (Fig. 7). The dark areas present near the starting line on both the radioautograms are artifacts caused by previous exposure of the unused film to I^{131} chromatograms. That these are artifacts is evidenced by the boundaries of the dark areas extending beyond the width of the chromatograms.

Discussion. Doctor and Trunnell(1) reported the presence of "extraneous" bands in

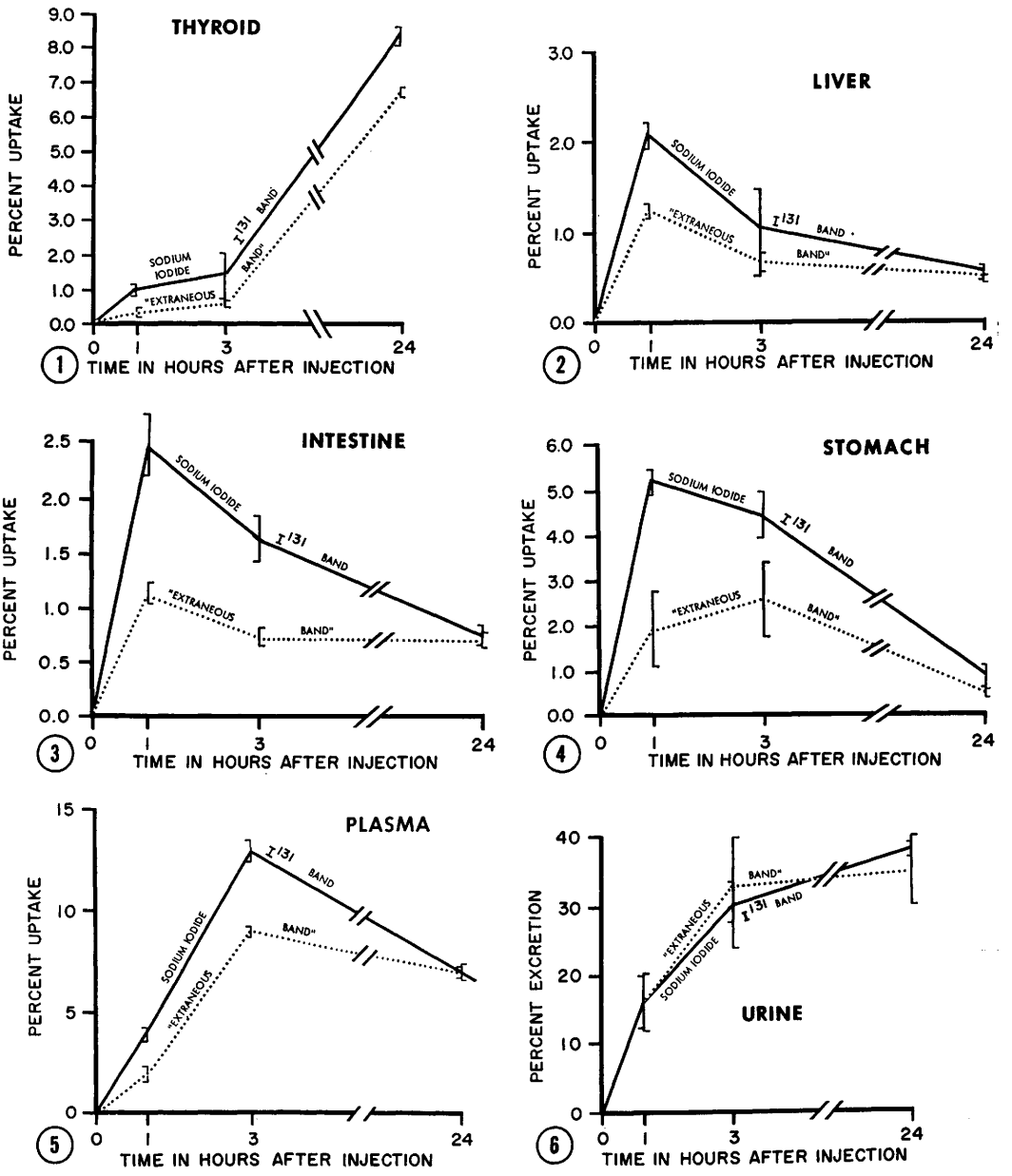

FIG. 1. Rate of uptake of NaI^{131} or "extraneous" I^{131} by thyroid gland. Results plotted are avg uptake with stand. errors on the whole thyroid gland. See text for details.

FIG. 2. Rate of uptake of NaI^{131} or "extraneous" I^{131} by the liver. Results plotted are avg uptakes with stand. errors for the entire liver. See text for details.

FIG. 3. Rate of uptake of NaI^{131} or "extraneous" I^{131} by the intestine. Results plotted are avg uptakes with stand. errors on the entire organ. See text for details.

FIG. 4. Rate of uptake of NaI^{131} or "extraneous" I^{131} by the stomach. Results plotted are avg uptakes with stand. errors on the entire organ. See text for details.

FIG. 5. Rate of uptake of NaI^{131} or "extraneous" I^{131} by plasma. Results plotted are avg uptakes with stand. errors for total plasma volume. See text for details.

FIG. 6. Rate of urinary excretion of NaI^{131} or "extraneous" I^{131}. Results plotted are avg excretions of I^{131} with stand. errors for the total urine collection. See text for details.

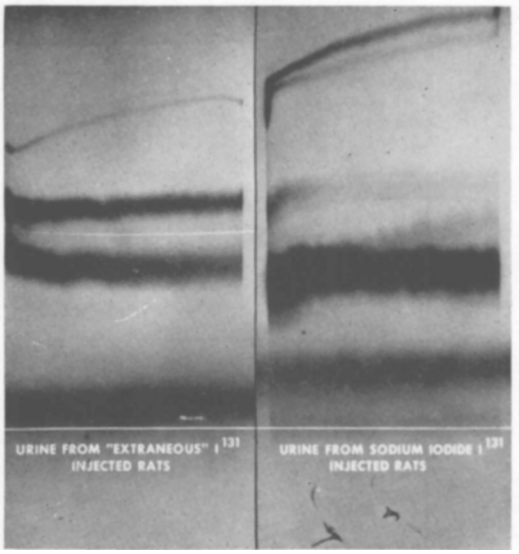

FIG. 7. Radioautograms of 1-hr urine samples from rats inj. with NaI^{131} or ''extraneous'' I^{131}. See text for details. The white line near the bottom and running across both radioautograms is the starting line. However, the white line in the middle of the radioautogram of 1-hr urine samples from ''extraneous'' I^{131} inj. rats is caused by a scratch on the X-ray film.

several batches of aged solutions of radioiodide received from Abbott Radio-Pharmaceuticals or from E. R. Squibb & Sons. It was also reported(1) that addition of 40 mg/ml of cysteine eliminated "extraneous" I^{131} material from these radioiodide solutions. The results on the biological properties of one of the major I^{131} contaminants were reported by Doctor(4). This compound, which moves slightly faster than NaI^{131} on paper chromatograms, was isolated by elution of the band from developed and air-dried radioautograms. Injection of eluates of "extraneous" I^{131} collected only 22% of the injected radioactivity in the thyroid of day-old chicks in contrast to almost 55% uptake observed following injection of chromatographically pure iodide-I^{131}.

Ahn and Rosenberg(2) reported that prior to March 1960 radioiodide solutions obtained from E. R. Squibb & Sons contained an average of 50% of the total radioactivity in iodide-I^{131} and similar preparations obtained from Abbott Radio Pharmaceuticals contained an average of 33% of the total radioactivity in iodide-I^{131}. The remaining portion of the radioactivity was present in an anionic component designated "S". Taurog (3) stored diluted (1:6 with water) Oak Ridge solutions of NaI^{131} without further addition of a reducing agent and reported the formation of unknown "U" to the extent of 50% of total I^{131} at the end of 27 days. It was reported in both of these papers(2,3) that since March 1960, the Squibb and the Abbott radioiodide preparations contain cysteine hydrochloride and that the products no longer show the presence of "extraneous" I^{131} or component "S" of Ahn and Rosenberg(2) or "U" of Taurog(3). However, Ahn and Rosenberg(2) reported that the effectiveness of cysteine hydrochloride in maintaining the chromatographic purity of commercially available radioiodide solutions may not be caused by its reducing properties. It was pointed out that the pH of a 0.2% solution of cysteine hydrochloride is 2.2 and that radioiodide preparations acidified to pH 3.0 with mineral acids are also reported(3,4) to show most of the radioactivity in iodide-I^{131}. Further, cysteine hydrochloride solutions (0.2%) neutralized to pH 6 were not effective in converting non-iodide impurities to iodide(2). Thus the question as to which is the best reducing agent and how much should be added to prevent the formation of the "extraneous" I^{131} is unanswered.

Squibb Iodotope (NaI^{131}) is obtained from the Canadian Atomic Energy Source and is made by irradiation of tellurium^{130}. This preparation is presumed to contain sodium bisulfite which is used for trapping the distilled I^{131} and to convert it to NaI^{131}. However, the Abbott NaI^{131} preparations are obtained from Oak Ridge I^{131} which is prepared by the fission of uranium. This preparation is NaI^{131} in basic sodium sulfite solution. Lantos and Tremezzani(7) reported absence of "extraneous" bands in radioiodide solutions obtained from Radiochemical Center of Amersham, England and which are reported to contain sodium thiosulfate.

The results presented here show that at 1 and 3 hours following injection of one microcurie of NaI^{131} or "extraneous" I^{131} into rats, the uptake of NaI^{131} by stomach, thyroid, liver, intestine and plasma was significantly

higher than the uptakes of "extraneous" I^{131}. These results clearly show that "extraneous" I^{131} is not immediately converted to NaI^{131} because of its dilution by body iodide or because of the presence of reducing agents in the tissues in accordance with the suggestion of Pitt-Rivers and Wolff(6). The results on the rate of uptake of NaI^{131} by rat organs and body fluids confirm an earlier report by Perlman *et al.*(8). Further, a close similarity between the rate of uptake curves for "extraneous" I^{131} and NaI^{131} may indicate that the 2 compounds are closely related and that there may be a gradual conversion of "extraneous" I^{131} into NaI^{131}. Fifty percent of the total I^{131} present in the one hour urine samples of rats receiving "extraneous" I^{131} was in the form of "extraneous" I^{131}. This would indicate that "extraneous" I^{131} is not completely reduced to iodide in a manner similar to that reported for iodate(9).

Summary. An "extraneous" I^{131} component identical with component "S" of Ahn and Rosenberg or "U" of Taurog was isolated from cysteine-free radioiodide preparations (obtained from E. R. Squibb & Sons) by a chromatographic separation and elution procedure described earlier.

One microcurie of NaI^{131} or of "extraneous" I^{131} were injected intraperitoneally into adult female rats. At the end of 1, 3 and 24 hours after injection, the animals were killed and the uptake of radioactivity in various organs and body fluids was measured. The results show that at one and 3 hours following injection, the uptake of NaI^{131} by stomach, thyroid, liver, intestine and plasma was significantly higher than the uptake of "extraneous" I^{131}. However, during the same period, urinary excretion of both the compounds remained the same. At 24 hours following injection of either NaI^{131} or "extraneous" I^{131} there was a significant lowering of radioactivity in stomach, liver, intestine and plasma and there were no significant differences in uptake of NaI^{131} or "extraneous" I^{131}. However, the thyroid gland continued to show an increased uptake of both NaI^{131} and "extraneous" I^{131} at 24 hours and also a significantly higher uptake of NaI^{131} in comparison to "extraneous" I^{131}. The results on the radioautography of one-hour urine samples from rats receiving an injection of "extreneous" I^{131} showed the presence of "extraneous" I^{131} to the extent of 50% of total I^{131} excreted. This would indicate that "extraneous" I^{131} is not rapidly reduced to iodide in a manner similar to that reported for iodate.

1. Doctor, V. M., Trunnell, J. B., *Endocrinology,* 1959, v64, 455.
2. Ahn, C. S., Rosenberg, I. N., *ibid.,* 1961, v68, 50.
3. Taurog, A., *ibid.,* 1961, v69, 126.
4. Doctor, V. M., *ibid.,* 1960, v66, 559.
5. Doctor, V. M., Rose, R. G., Dewey, W. C., *ibid.,* 1960, v67, 875.
6. Pitt-Rivers, R., Wolff, J., *ibid.,* 1959, v64, 841.
7. Lantos, C. P., Tramezzani, J. H., *Acta Physiol. Latinoamer.,* 1961, v11, 1.
8. Perlman, I., Chaikoff, I. L., Morton, M. E., *J. Biol. Chem.,* 1941, v139, 433.
9. Leblond, C. P., Süe, P., *Am. J. Physiol.,* 1941, v134, 549.

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Effect of Stable Cesium on the Retention of Cesium^{137} by Rats.* (27461)

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Because Cs^{137} is one of the potentially more hazardous products of nuclear fission, many attempts have been made to accelerate its excretion from animals. The list of materials tested with varying degrees of success or failure includes stable potassium(1,2), stable potassium and sodium(3), hormones and diuretics(4), enzyme inhibitors(5), ver-

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