A ^{99m}Tc-CHELATE SUBSTITUTE FOR ORGANORADIOMERCURIAL RENAL AGENTS

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Dimercaptosuccinate has been labeled with ^{99m}Tc-pertechnetate for imaging renal cortical morphology. Following intravenous administration, its in vivo kinetics mimic that of ^{203}Hg-chlormerodrin.

Mercury-203-labeled diuretic agents have proven useful for imaging renal cortical morphology. Unfortunately, their high absorbed radiation dose has limited their utility. A nontoxic ^{99m}Tc-labeled agent with similar in vivo distribution properties would allow for significant diminution in absorbed radiation dose permitting administration of larger activities with resultant increase in resolution. Technetium-99m-Sn DTPA preparations behave as though they were a measure of glomerular filtration, and activity is not retained in the renal cortex. Thus their use in static imaging of renal cortical morphology is limited. Technetium-99m-Sn saccharides do localize to a degree in the renal cortex, but they are also largely excreted in the urine and cannot be considered homologs of organoradiomercurial renal agents.

We have developed a series of ^{99m}Tc-labeled mercaptocarboxylates whose in vivo distribution kinetics mimic that of ^{203}Hg-chlormerodrin. One of these agents, Sn-dimercaptosuccinic acid, is now available in kit form, and its preclinical evaluation is the subject of this communication. When $^{99m}TcO^{-}_{4}$ is mixed with an equal part of a solution of 1 m*M* $SnCl_2$ (0.19 mg/ml) and 3 m*M* dimercaptosuccinic acid (0.547 mg/ml), labeling is rapid. Following intravenous administration of the labeled chelate to dogs, the initial distribution is approximately the plasma volume with the label bound to plasma proteins, negligible quantities being found on RBC. Initial plasma clearance proceeds with a $T_{1/2}$ of approximately 45 min, due almost exclusively to renal accumulation of activity. Serial whole-body scintigraphy in the dog is shown in the upper portion of Fig. 1. In vivo scintigraphy using a 4,000-hole and a pinhole collimator is shown in the center of the figure. Activity is confined to the renal cortex as shown in the scintiphoto

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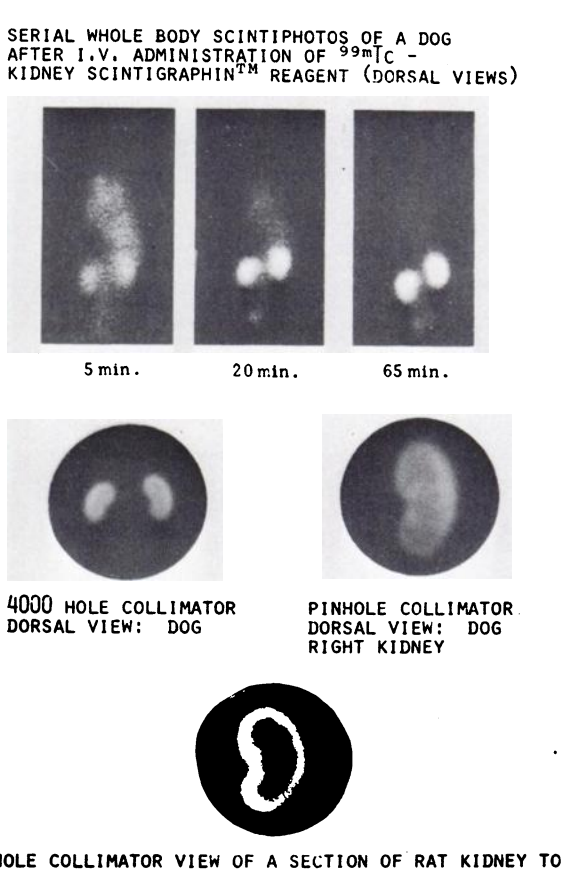

FIG. 1. Accumulation of ^{99m}Tc-Sn-dimercaptosuccinate in renal cortex of dog and rat.

of a slice of rat kidney in the lower portion of the figure. The percent of administered dose localized in rat tissues 1 hr after intravenous administration of the ^{99m}Tc complex are: kidneys 54.2 $\pm$ σ = 21%, urine and urinary bladder 7.2 $\pm$ σ = 1.7%, liver and spleen 5.3 $\pm$ σ = 0.9%, whole blood 19%, and the remainder of the body 12.5%. This distribution is comparable to that reported for ^{203}Hg-chlormerodrin (*1*). Dimercaptosuccinate has been administered parenterally in gram quantities to humans in the treatment of heavy metal poisoning (*2*) and its LD_{50} given through the intraperitoneal route to mice is reported as 3.163 gm/kg (*3*).

Rats given 1.21 ml/kg of the Sn-dimercaptosuccinate reagent (MPI Kidney Scintigraphin Reagent) intravenously for 14 consecutive days failed to show any clinical or histologic changes related to administration of the reagent. Dogs given 0.31 ml/kg of reagent diluted 1:1 with normal saline solution (0.62 ml/kg of diluted reagent) intravenously for 17 consecutive days failed to show any clinical abnormalities or significant changes in serum calcium, inorganic phosphorus, glucose, BUN, uric acid, cholesterol, total protein, albumin, total bilirubin, alkaline phosphatase, LDH, and SGOT during such administration and for approximately 2 weeks thereafter when the study was terminated. Dogs sacrificed after 17 consecutive days of administration of the reagent as noted above failed to show any gross pathological or histologic changes related to administration of the material.

Preliminary clinical studies suggest in vivo behavior in humans comparable to that noted in animal studies. Our results suggest that ^{99m}Tc-labeled Sn-dimercaptosuccinate may replace the use of organoradiomercurial agents in the study of renal cortical morphology and possibly may find usefulness in evaluation of brain abnormalities as have the radiomercurial agents in the past.

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