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Uptake of Technetium-99m-Tetrofosmin, Technetium-99m-MIBI and Thallium-201 in Tumor Cell Lines

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We investigated the kinetics, cellular uptake and intracellular distribution of ^{99m}Tc-tetrofosmin in tumor cell lines and compared them with those of ^{99m}Tc-MIBI and ^{201}Tl. **Methods:** At specific intervals after incubation with radiotracers, cellular uptake was determined. Cells were also treated with nigericin, carbonyl cyanide m-chlorophenylhydrazone (CCCP) and ouabain to determine their effects on the uptake of the tracers. **Results:** Each tracer showed similar uptake kinetics in both cell lines, and a steady-state was maintained for at least 4 hr. Nigericin stimulated the uptake of both ^{99m}Tc-tetrofosmin and ^{99m}Tc-MIBI in HBL-2 cells, although it inhibited their uptake in SW-13 cells. Nigericin also inhibited 90% of ^{201}Tl uptake in both cell lines. Addition of CCCP caused 73%–97% release of accumulated ^{99m}Tc-MIBI from both cell lines with or without nigericin pretreatment, indicating that most of the accumulated ^{99m}Tc-MIBI was related to mitochondria. The effect of CCCP on accumulated ^{99m}Tc-tetrofosmin was less marked than that on ^{99m}Tc-MIBI in both cell lines, indicating that only a part of accumulated ^{99m}Tc-tetrofosmin, was related to mitochondria. Ouabain preincubation inhibited 74%–77% and 51%–53% of ^{201}Tl uptake in HBL-2 and SW-13 cells, respectively, as well as inhibited 22%–31% uptake of ^{99m}Tc-tetrofosmin in both HBL-2 and SW-13 cells. Uptake by the dead cells of either cell line was negligible for each tracer. **Conclusion:** Technetium-99m-tetrofosmin uptake depends on both cell membrane and mitochondrial potentials. Only a small fraction of ^{99m}Tc-tetrofosmin accumulates inside the mitochondria, while most ^{99m}Tc-MIBI accumulates inside the mitochondria. Thallium-201 uptake is partly independent of the Na^+, K^+ pump.

Key Words: tumor cell lines; technetium-99m-tetrofosmin; technetium-99m-MIBI; thallium-201; mitochondrial and cell membrane potentials

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Thallium-201 chloride and technetium-99m-hexakis-isobutyl-isonitrile (^{99m}Tc-MIBI) are widely used as myocardial perfusion agents (*1–4*). Both agents have also shown potential utility in the detection of various tumors (*5–8*). However, the uptake mechanisms of these agents differ. The uptake of ^{201}Tl to myocardial and tumor cells is related to cell membrane potential and Na^+K^+ ATPase activity (*9–12*). On the other hand, that of ^{99m}Tc-MIBI to these cells is also related to cell membrane potential, although passage through this membrane involves passive diffusion (*13–15*). Furthermore, the behaviors of these agents inside the cells also differ. Technetium-99m-MIBI is localized mostly inside mitochondria due to negative mitochondrial membrane potential, whereas ^{201}Tl remains in the cytosolic compartment (*9–16*). Technetium-99m-ethylene-bis[bis(2-ethoxyethyl) phosphin] (^{99m}Tc-tetrofosmin), a newly developed compound of the diphosphin group, like ^{201}Tl and MIBI, is currently used as a myocardial perfusion agent (*17,18*) and may be utilized to detect various tumors. It is a monovalent lipophilic cation that rapidly enters the myocardial cells due to its lipophilic properties (*17,19*), although this property alone may not be the sole determinant.

The purposes of this study were to evaluate the uptake kinetics of ^{99m}Tc-tetrofosmin in tumor cell lines and to compare them with those of ^{99m}Tc-MIBI and ^{201}Tl. For this purpose, three chemical agents were used: nigericin, an ionophore that increases the mitochondrial membrane potential and disrupts the cell membrane potential (*20,21*); carbonyl cyanide m-chlorophenylhydrazone (CCCP), an uncoupler of oxidative phosphorylation that depolarizes the mitochondrial membrane potential (*22*); and ouabain, a cell membrane Na^+, K^+ ATPase inhibitor (*23*).

MATERIAL AND METHODS

Cell Lines

The Epstein-Barr virus-negative lymphoma B-cell line HBL-2 (*24*) was cultured in RPMI 1640 (contained in m*M*, $Ca(NO_3)_2$, 0.42; $MgSO_4$, 0.4; KCl, 5.36; $NaHCO_3$, 11.9; NaCl, 102.67; Na_2HPO_4, 5.36) supplemented with heat-inactivated 20% fetal bovine serum (FBS) and antibiotics (penicillin 10 IU/ml and streptomycin 50 μg/ml). Cells were cultured as suspensions in 225 cm^2 tissue culture flask in the growth medium at 37°C in a humidified 5% CO_2/95% air atmosphere. After priming for 1 wk with addition of new medium on alternate days, the cells were harvested by centrifugation at 1000 rpm for 1–2 min and then washed with fresh FBS-free medium. The cells were resuspended at a concentration of 1×10^6/ml in FBS-free medium, transferred to plastic tubes and kept at 37°C for at least 1 hr for equilibration. All tubes were pretreated with 0.5% bovine serum albumin (BSA) to minimize adhesion of the tracers to the surface of the tubes.

The small-cell carcinoma of the adrenal cortex cell line, SW-13 (*25*), was obtained commercially. The cells were cultured to

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confluence in a 225 cm^2 tissue culture flask in L-15 medium (in m*M*, $CaCl_2$, 1.67; $MgCl_2$, 2.1; $MgSO_4$, 0.81; KCl, 5.36; KH_2PO_4, 0.44; NaCl, 136.89; Na_2HPO_4, 1.34) supplemented with 10% heat-inactivated FBS and antibiotics (penicillin 10 IU/ml and streptomycin 50 μg/ml) at 37°C in CO_2 free atmosphere at a pH 7.4–7.6. After harvesting with 0.25% trypsin and washed with fresh medium, the cells were transferred to 35-mm cell culture wells at 4×10^5 cells per well in 4 ml of medium and kept at 37°C in humidified 5% CO_2/95% air atmosphere for 48 hr. After 48 hr, the medium was replaced with 1 ml of freshly prepared FBS-free L-15 medium and kept for 30 min for equilibration. The number of cells in each 2–3 wells was counted and the average value was used. All uptake values were normalized to 1×10^6 cells.

Preparation of Dead Cells

Dead cells of both HBL-2 and SW-13 were prepared by mixing 100–200 m*M* of sodium cyanide in tubes containing cells (usually $>10^7$) and incubating for 24–48 hr in hypoxic state. Tryphan blue dye exclusion revealed that 100% of the cells were dead. Dead cells were incubated in the same way as corresponding live cells except that, after 1 hr of incubation with radiotracer, the dead SW-13 cell suspension was transferred into test tubes and treated like those of HBL-2 for determination of cell-associated activity.

Preparation of Radiotracers

We used tetrofosmin as a lyophilized kit preparation. Each vial contains 230 μg tetrofosmin. After labeling with 185–370 MBq ^{99m}Tc-pertechnetate, the labeling efficiency was determined (*26*) and it was always more than 90%. Technetium-99m-tetrofosmin was diluted with saline to obtain 1 μg of ^{99m}Tc-tetrofosmin in 100 μl of labeled solution that was added to each tube or well containing cell lines.

Prelabeled ^{99m}Tc-MIBI was obtained commercially. The labeling efficiency was determined (*11*), which was more than 95%. One milliliter of labeled compound contained 500 μg ^{99m}Tc-MIBI and was diluted to obtain 1 μg ^{99m}Tc-MIBI in 100 μl of solution; this was added to each tube or well of cell lines.

Thallium-201 was diluted with saline to 111–148 KBq (3–4 μCi) per 100 μl of solution, which was added to each tube or well containing cell lines.

Uptake Studies

All experimental samples were made in triplicate and most of the experiments were repeated 2–3 times. To determine the nonspecific uptake at the side walls of the tubes or residual fluid activity in the wells, at least 3 tubes or wells without cells were treated in the same way as the tubes and wells containing cells in each experimental batch. The average activity was considered as the nonspecific or residual fluid activity for that batch. After incubation with radiotracers, tubes containing HBL-2 were centrifuged at 1000 rpm for 1–2 min and washed quickly once with FBS-free RPMI 1640 medium and the supernatant was discarded. The tubes containing sediment cells were counted by an auto gamma-well counter. Wells containing SW-13 were washed once with FBS-free L-15 medium after incubation for the same time intervals as HBL-2, then cells were harvested by 0.25% trypsin, transferred into tubes, and counted with the same gamma-well counter.

Evaluation of Uptake Kinetics. Both cell lines were incubated with radiotracers for 10, 30, 60, 120, 180 and 240 min. After these incubation periods, cells were collected and counted for radioactivity.

Evaluation of Nigericin Effect. Both cell lines were preincubated with 5 μg nigericin for 15 min before the addition of radiotracers. The incubation time with the radiotracers was 60 min.

Evaluation of CCCP Effect. After 55 min of incubation with radiotracers in both cell lines, 10 μ*M* (final concentration) CCCP was added to the medium (cells under basal condition and cells after preincubation with nigericin for 15 min) and incubation was continued for 5 min. Both nigericin and CCCP were dissolved in DMSO with the final concentration of DMSO in each preparation being less than 0.5%.

Evaluation of Ouabain Effect. Both cell lines were pre-incubated with 100 μ*M* (final concentration) ouabain for 15 or 30 min and then incubated with radiotracers for 60 min.

After pre-incubation with chemical agents, the cell viability was checked by tryphan blue dye exclusion technique and compared with that of control cells in each experiment.

Electron Microscopic Study

Analysis of cell preparation was performed, using standard procedures (*27*), under an electron microscope to determine the density of mitochondria in both HBL-2 and SW-13 cell lines.

Data Analysis

Net uptake in the cells (both alive and dead) was expressed as a percent of the dose added to the tubes or wells after subtracting the corresponding average nonspecific or residual fluid activity in the tubes or wells, respectively. The net uptake after various chemical challenges was expressed as a percent of 1-hr uptake values obtained in the control for that batch. Data were expressed as the mean plus or minus standard error of mean (s.e.m) unless otherwise stated. The significance was assessed by one-way analysis of variance and a p value of less than 0.05 was considered significant.

RESULTS

Uptake Kinetics

Figure 1 shows the uptake kinetics of ^{99m}Tc-tetrofosmin, ^{99m}Tc-MIBI and ^{201}Tl in both HBL-2 and SW-13 cell lines. Each radiotracer showed similar uptake kinetics in both cell lines. The uptake value of each tracer gradually increased during the first hour and reached a plateau by 1 hr which was maintained for at least 4 hr. Compared to that of ^{99m}Tc-MIBI or ^{201}Tl, the net uptake of ^{99m}Tc-tetrofosmin was lower in both HBL-2 and SW-13. However, the net uptake values of all the tracers were higher in SW-13 than in HBL-2. The uptake of ^{201}Tl in SW-13 was the highest.

Effect of Nigericin

Figure 2 shows the effect of nigericin on the 1-hr uptake of ^{99m}Tc-tetrofosmin, ^{99m}Tc-MIBI and ^{201}Tl in both cell lines. In HBL-2, nigericin stimulated the uptake of both ^{99m}Tc-tetrofosmin and ^{99m}Tc-MIBI, but that of ^{99m}Tc-MIBI was significantly higher ($p < 0.05$) than that of ^{99m}Tc-tetrofosmin. In SW-13, however, there was inhibition of ^{99m}Tc-tetrofosmin and ^{99m}Tc-MIBI uptake. In both cell lines, almost 90% inhibition of ^{201}Tl uptake was observed after nigericin preincubation.

Effect of Ouabain

The effect of preincubation with ouabain is shown in Table 1. There was approximately 74%–77% inhibition of ^{201}Tl uptake in HBL-2, though only 51%–53% inhibition was observed in SW-13. Approximately 22%–31% inhibition of ^{99m}Tc-tetrofosmin uptake was observed in both HBL-2 and SW-13 cell lines. In the HBL-2 cell line, no change of ^{99m}Tc-MIBI uptake was observed after a 15-minute preincubation, but it was moderately increased by a 30-minute preincubation. However, 21%–26% inhibition of ^{99m}Tc-MIBI uptake was observed in SW-13 cells. The inhibition by ouabain of the uptake of ^{99m}Tc-tetrofosmin in HBL-2 cells was significantly different from that of ^{99m}Tc-MIBI.

Effect of CCCP

The effect of CCCP is also shown in Table 1. After addition of CCCP, only 33% release was seen of the accumulated

^{99m}Tc-tetrofosmin in the basal condition (without nigericin), but 85% release was observed with nigericin preincubated HBL-2 cells, while a 21% and 35% release was observed in SW-13 cells with and without nigericin preincubation, respectively. There was 73% to 97% release of the accumulated ^{99m}Tc-MIBI observed in both cell lines with and without nigericin preincubation. There was no significant effect observed on the uptake of ^{201}Tl in HBL-2 or SW-13 cells without nigericin. The effect of CCCP on ^{201}Tl uptake could not be ascertained after nigericin preincubation because of the effect of nigericin, which caused almost 90% inhibition of ^{201}Tl uptake in both cell lines (Fig. 2).

Figure 3 shows the mitochondrial density in each cell line as observed under electron microscopy. The number of mitochondria was larger in SW-13 than in HBL-2.

The uptake in dead cells was without exception negligible and was in some batches lesser than the activity constituted at the side walls. Cell viability did not significantly differ among controls or cells after chemical challenges, and the cell viability was always >90%.

DISCUSSION

The uptake of ^{99m}Tc-MIBI into cells has been postulated to be energy-dependent, and accumulation is observed mostly inside the mitochondria due to the negative membrane potential, while passage through the cell membrane is related to passive diffusion (*14–16*). The uptake of ^{201}Tl into the cell is related to cell membrane potential and Na^+K^+ ATPase activity, but, inside the cell, ^{201}Tl remains in the cytosolic compartment (*9–12*). Technetium-99m-tetrofosmin, a newly developed lipophilic cation for myocardial perfusion, is now in use in clinical myocardial studies (*17,18,28*). To investigate the kinetics of ^{99m}Tc-tetrofosmin in tumor cell lines, we selected HBL-2 and SW-13 cell lines because of their differing mitochondrial densities (*29*). The uptake kinetics and possible mechanisms of uptake of ^{99m}Tc-tetrofosmin were compared with those of ^{99m}Tc-MIBI and ^{201}Tl.

Each tracer showed similar uptake kinetics in both cell lines, and the pattern of accumulation was in agreement with that delineated in other reports (*12,30*). All tracers showed higher accumulation in the SW-13 than in HBL-2 cell line. The higher uptake of ^{99m}Tc-tetrofosmin and ^{99m}Tc-MIBI might be related to the larger number of mitochondria in the SW-13 cell line observed by electron microscopy, which may have caused increased metabolic activity and negative mitochondrial membrane potentials, as suggested by previous investigators (*15*). The higher uptake of ^{201}Tl also might be due to increased cell membrane potential and increased Na^+K^+ ATPase activity. Although the net uptake of ^{99m}Tc-tetrofosmin was lower than that of either ^{99m}Tc-MIBI or ^{201}Tl, it maintained a plateau similar to that for ^{99m}Tc-MIBI and ^{201}Tl for at least 4 hr. This indicates that ^{99m}Tc-tetrofosmin forms a steady-state with the medium in a manner similar to ^{99m}Tc-MIBI and ^{201}Tl. There was no uptake of tracers to the dead cells, which is in agreement with the observation of other investigators (*11,13*). This might indicate that there was no binding to the cell membranes or hydrophobic regions of cell membrane protein, as was seen in another myocardial agent (*11*). Uptake of these tracers would be solely by the viable and metabolically active cells. Technetium-99m-tetrofosmin did not show any uptake to the dead cells either, indicating that uptake was solely by viable cells, like that of ^{99m}Tc-MIBI or ^{201}Tl.

Nigericin, which causes secondary increase of mitochondrial inner membrane potential and disruption of the cell membrane potential (*20,21*), induced increased accumulation of both

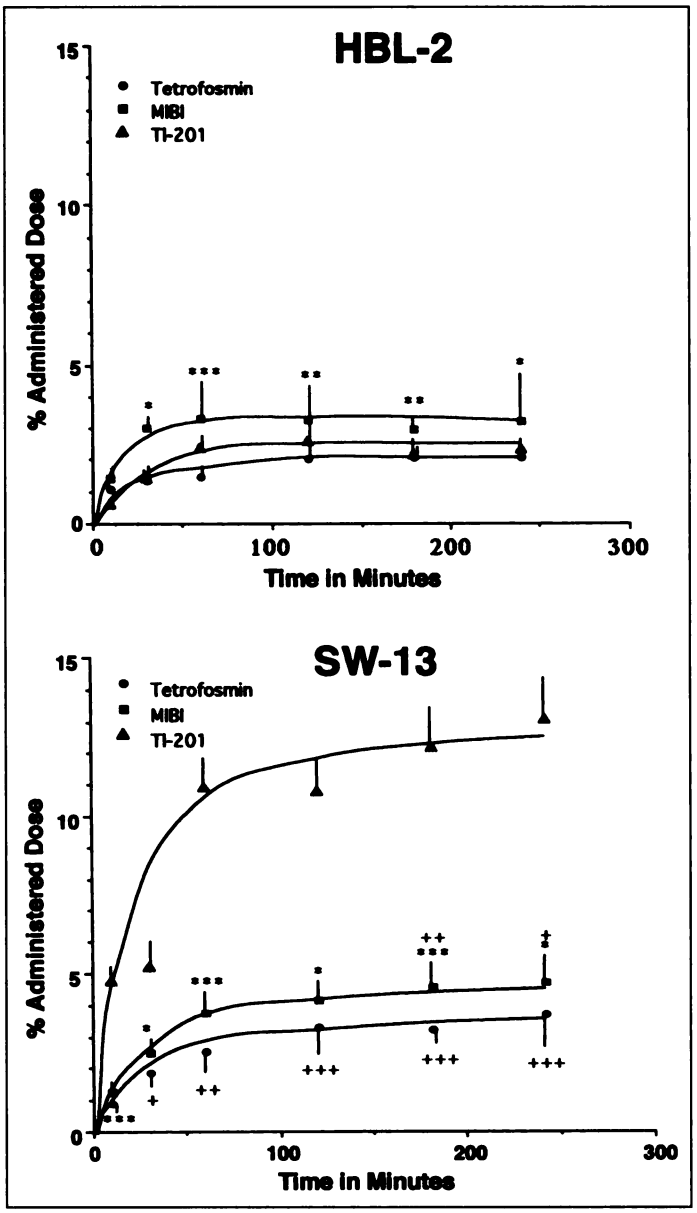

FIGURE 1. Uptake kinetics of ^{99m}Tc-tetrofosmin, ^{99m}Tc-MIBI and ^{201}Tl in HBL-2 and SW-13 cell lines. The mean ± 1 s.d. (each symbol represents 3–9 measurements) are shown. Lines were drawn manually. Uptake value of each tracer gradually increased during the first hour and plateaued by 1 hr which was maintained for at least 4 hr. Note high uptake of ^{201}Tl in SW-13 cells compared to that of the other two tracers. The uptake of ^{99m}Tc-MIBI was significantly higher than that of ^{99m}Tc-tetrofosmin in both cell lines. *Significant difference between ^{99m}Tc-MIBI and ^{99m}Tc-tetrofosmin. $^+$Significant difference between corresponding HBL-2 and SW-13 cells. */+ = $p < 0.05$, **/++ = $p < 0.01$, ***/+++ = $p < 0.001$.

^{99m}Tc-MIBI and ^{99m}Tc-tetrofosmin in the HBL-2 cells, although it inhibited the uptake of both these tracers in SW-13 cells. However, after addition of CCCP, which depolarizes the mitochondrial membrane potential (*22*), there was almost 73%–78% release of accumulated ^{99m}Tc-MIBI from the control and 94%–97% release from the nigericin preincubated cells in both cell lines, indicating selective accumulation of ^{99m}Tc-MIBI in the mitochondria. These findings are in agreement with those of other investigators and suggest that more than 90% of the total ^{99m}Tc-MIBI taken up in myocardial cells accumulates in the mitochondria (*13,14,16*). Technetium-99m-tetrofosmin also showed a similar tendency towards increased accumulation after nigericin preincubation in HBL-2 cells, but there was a significant difference between ^{99m}Tc-MIBI and ^{99m}Tc-tetrofos-

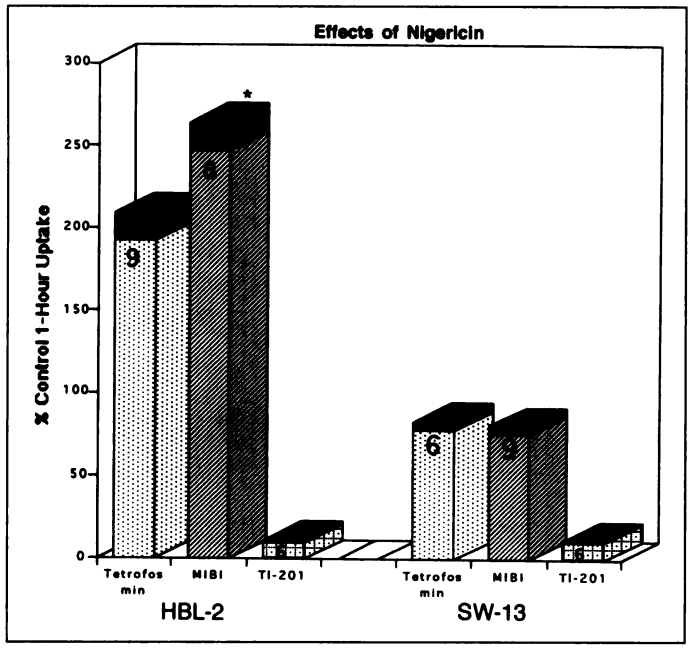

FIGURE 2. Effect of nigericin preincubation on the uptake at 1 hr. Black area at top of each column represents s.e.m. Number shown in each column represents number of measurements. In HBL-2 cells, ^{99m}Tc-MIBI showed significantly ($p < 0.05$) higher %-control-1-hr uptake than ^{99m}Tc-tetrofosmin. Note that 90% inhibition of ^{201}Tl uptake was induced by nigericin preincubation. *Significant difference between ^{99m}Tc-MIBI and ^{99m}Tc-tetrofosmin.

min uptakes (Fig. 2). After CCCP challenge, there was 33% release from the HBL-2 cells without preincubation with nigericin and 85% release from those with nigericin preincubation, but only 21% and 35% release was observed in the SW-13 cells with and without nigericin preincubation, respectively. These findings might indicate that only a fraction of ^{99m}Tc-tetrofosmin, unlike ^{99m}Tc-MIBI, inside the cells is related to mitochondrial accumulation and that most ^{99m}Tc-tetrofosmin accumulates in the cytosolic fraction. However, the mitochondrial potential plays certain roles in the uptake of ^{99m}Tc-tetrofosmin, which are apparent after nigericin preincubation and which also have been suggested by other investigators (*31*). The inhibition of the uptake of both tracers in SW-13 cells after nigericin preincubation and the relatively mild effect of CCCP on ^{99m}Tc-tetrofosmin uptake might be due to the different characteristics of these cell lines rather than an effect of the medium, as further investigation using RPMI-1640 medium has failed to disclose any change of uptake pattern (unpublished data). This might be due to difference in the permeability to cations in different cell lines. The uptake of these tracers in SW-13 cells might be related to the Na^+, K^+ pump, and disruption of this pump after nigericin preincubation might cause decreased uptake, as both cell lines also showed poor uptake of ^{201}Tl after nigericin preincubation due to the latter's effects on cell membrane potential (*21*).

Preincubation with ouabain, a cell membrane Na^+, K^+ ATPase inhibitor (*23*), inhibited ^{201}Tl uptake by 74%–77% and 51%–53% in HBL-2 and SW-13 cells, respectively. The remaining 25% of ^{201}Tl uptake in HBL-2 might be independent of the Na^+, K^+ pump, as has also been suggested by others (*9,11*). Approximately 50% of remaining ^{201}Tl accumulated in SW-13 might accumulate either due to the presence of excess cations in the L-15 medium or difference in cell model or due to the presence of strong Na^+, K^+ pump, which was not completely blocked by the doses of ouabain used. In an experiment, Brismar et al. (*32*) found different ouabain-sensitive fraction of ^{201}Tl uptake in a cell line in different medium. In another experiment with human glioma cells, Brismar et al. (*12*) found that ouabain produced inhibition only 40% of control uptake of ^{201}Tl and that ^{201}Tl uptake was inversely related to external concentration of potassium (K^+). They also showed that exter-

TABLE 1
Effects of Pretreatment with Ouabain for 15 and 30 Minutes and Addition of CCCP to Cells with and without Nigericin Preincubation

Conditions	^{99m}Tc-tetrofosmin	^{99m}Tc-MIBI	^{201}Tl
HBL-2 cells			
Ouabain, 15 min	77.4 ± 4.4 (6)*‡	98.7 ± 5.2 (7)†	23.3 ± 2.3 (9)
	[22.6 ± 4.4]	[1.3 ± 5.2]	[76.7 ± 2.3]
Ouabain, 30 min	77.6 ± 6.2 (6)*§	129.4 ± 9.6 (6)	26.4 ± 3.6 (6)
	[22.4 ± 6.2]	[Stimulated]	[73.6 ± 3.6]
CCCP, without nigericin	66.9 ± 4.7 (6)*§	22.5 ± 7.2 (3)	90.3 ± 4.4 (6)
	[33.1 ± 4.7]	[77.5 ± 7.2]	[9.7 ± 4.4]
CCCP, with nigericin	15.4 ± 3.1 (9)*‡	3.4 ± 1.4 (8)	13.9 ± 0.7 (6)¶
	[84.6 ± 3.1]	[96.6 ± 1.4]	[86.1 ± 0.7]
SW-13 cells			
Ouabain, 15 min	69.1 ± 2.3 (6)	73.9 ± 3.7 (9)	48.7 ± 2.1 (6)
	[30.9 ± 2.3]	[26.1 ± 3.7]	[51.3 ± 2.1]
Ouabain, 30 min	77.0 ± 2.8 (6)	78.9 ± 3.0 (9)	46.8 ± 1.1 (6)
	[23.0 ± 2.8]	[21.1 ± 3.0]	[53.2 ± 1.1]
CCCP, without nigericin	79.4 ± 2.9 (6)*§	26.9 ± 5.7 (6)	98.9 ± 6.7 (6)
	[20.6 ± 2.9]	[73.1 ± 5.7]	[1.1 ± 6.7]
CCCP, with nigericin	65.4 ± 2.4 (9)*§	6.6 ± 1.6 (6)	10.6 ± 0.5 (3)¶
	[34.6 ± 2.4]	[94.4 ± 1.6]	[89.4 ± 0.5]

*Significant difference between ^{99m}Tc-tetrofosmin and ^{99m}Tc-MIBI. Significant difference between 15- and 30-min preincubation with ouabain.
†$p < 0.05$.
‡$p < 0.01$.
§$p < 0.001$.
¶Decreased uptake due to effect of nigericin (Fig. 2).
Data are expressed as mean ± s.e.m. of percentage of 1-hr uptake. Numbers in parentheses are the number of samples. Data in brackets are percentage of inhibition.

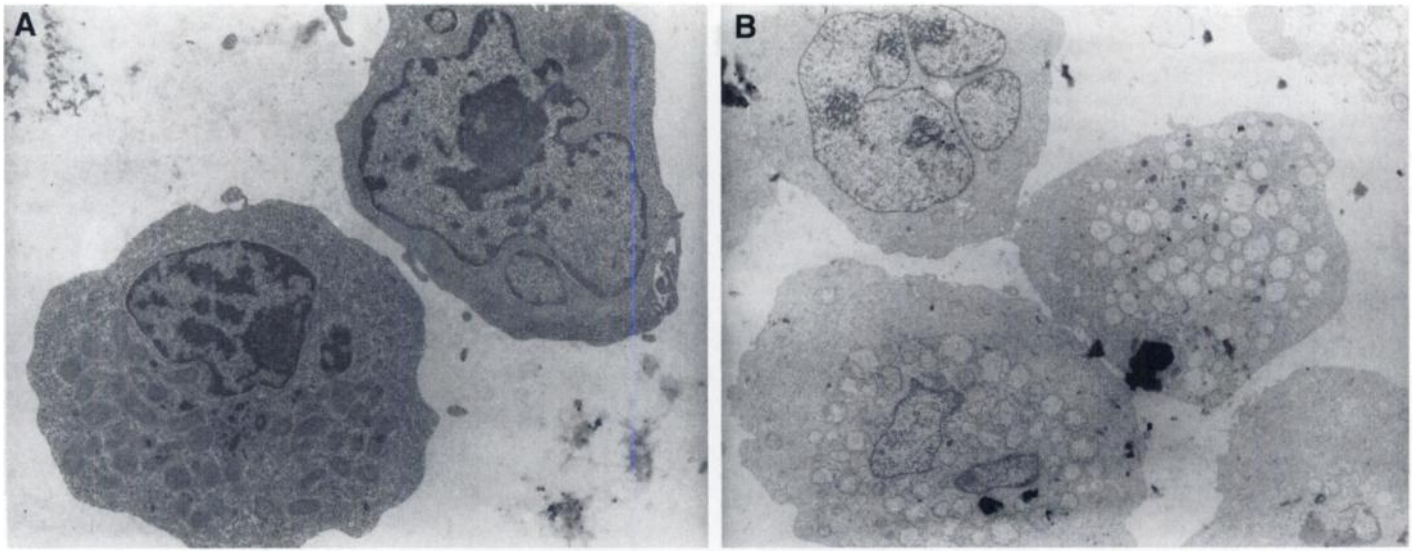

FIGURE 3. Electron microscopic appearance of (A) HBL-2 (6000×) and (B) SW-13 (2500×) cell lines. Note the greater mitochondrial density in the SW-13 cells.

nal cations other than K^+ also influenced ^{201}Tl uptake. Although we did not measure the cell membrane ATPase activity, we believe that a strong Na^+, K^+ pump might be indicated by the higher ^{201}Tl uptake in SW-13. There was no difference in ^{99m}Tc-MIBI uptake after 15-min preincubation with ouabain, but after 30 min, ^{99m}Tc-MIBI showed increased accumulation in HBL-2 cells. This phenomenon has also been shown in other investigations (*11,14*) and might be due to a relative increase in the mitochondrial potential due to disruption of the cell membrane potential that is maintained by the Na^+, K^+ pump. Technetium-99m-tetrofosmin showed decreased accumulation in both HBL-2 and SW-13 cells after ouabain preincubation at both 15 and 30 min. This indicates that 20%–30% of the uptake of ^{99m}Tc-tetrofosmin by the cells is dependent on the cell membrane Na^+, K^+ pump and can be blocked by ouabain. The lower uptake of ^{99m}Tc-MIBI in SW-13 cells after ouabain pretreatment might indicate that the uptake in these cells is partly related to the cell membrane Na^+, K^+ pump. In an experiment with neuroblastoma-glioma hybrid cell, Lichtshtein et al. (*33*) also found that, despite accumulation of lipophilic cation inside mitochondria, ouabain released the accumulated cations over long period of time. This suggests that the uptake of lipophilic cations might differ in different cell models.

In view of our results, it might be suggested that, like ^{99m}Tc-MIBI and ^{201}Tl, ^{99m}Tc-tetrofosmin can be used as a tumor imaging agent. However, the uptake of each of these agents would indicate different properties of the cell. Technetium-99m-MIBI would accumulate most in tumors with abundant mitochondria, ^{201}Tl in those with increased cell membrane potentials and ^{99m}Tc-tetrofosmin in those having either of these two features.

CONCLUSION

The uptake of the three tracers evaluated indicates cell viability. The uptake of ^{99m}Tc-tetrofosmin depends on both the cell membrane (Na^+,K^+ pump) and mitochondrial potential, and only a fraction of ^{99m}Tc-tetrofosmin accumulates inside mitochondria, while ^{99m}Tc-MIBI accumulates primarily inside mitochondria. Thallium-201 uptake by the cells is partly independent of Na^+, K^+ pump.

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FIRST IMPRESSIONS

What happened to the facial bones?
For acquisition information, see page 1582.