Glucose Transport and Glucose 6-Phosphate Hydrolysis in Intact Rat Liver Microsomes*

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Glucose transport was investigated in rat liver microsomes in relation to glucose 6-phosphatase (Glu-6-Pase) activity using a fast sampling, rapid filtration apparatus. 1) The rapid phase in tracer uptake and the burst phase in glucose 6-phosphate (Glu-6-P) hydrolysis appear synchronous, while the slow phase of glucose accumulation occurs during the steady-state phase of glucose production. 2) [14C]Glucose efflux from preloaded microsomes can be observed upon addition of either cold Glu-6-P or Glu-6-Pase inhibitors, but not cold glucose. 3) Similar steady-state levels of intramicrosomal glucose are observed under symmetrical conditions of Glu-6-P or vanadate concentrations during influx and efflux experiments, and those levels are directly proportional to Glu-6-Pase activity. 4) The rates of both glucose influx and efflux are characterized by values that are independent of Glu-6-P concentrations. 5) Glucose efflux in the presence of saturating concentrations of vanadate was not blocked by 1 mM phloretin, and the initial rates of efflux appear directly proportional to intravesicular glucose concentrations. 6) It is concluded that glucose influx into microsomes is tightly linked to Glu-6-Pase activity, while glucose efflux may occur independently of hydrolysis, so that microsomal glucose transport appears unidirectional even though it can be accounted for by diffusion only over the accessible range of sugar concentrations.

Given the peculiar localization of glucose 6-phosphatase (Glu-6-Pase) (EC 3.1.3.9) into the endoplasmic reticulum, the membrane topology of this enzyme has been controversial for many years. While most authors agree that the enzyme is an integral protein tightly associated with the hydrophobic part of the native membrane, as confirmed recently by the amino acid sequence inferred from the isolated cDNA encoding human (1)

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2 Corresponding to one of the four principal experimental situations that lend themselves well to kinetic analysis of transport processes as described for example in Ref. 25. Accordingly, in the experiments described, there was no glucose inside of the microsomes, the membrane side opposite (the trans face) to the uptake medium where the radiotracer was introduced (and defined as the cis face). Clearly, then, zero-trans experiments can be performed under influx and efflux conditions.

and mouse (2) Glu-6-Pases, there is no consensus to date as to whether the catalytic site is oriented toward the lumen of the endoplasmic reticulum or freely accessible from the cytoplasm. Two major but opposite models have thus emerged during the last 20 years.

In the substrate transport model (3–8), it is thought that glucose 6-phosphate (Glu-6-P) is hydrolyzed to glucose and phosphate in the lumen of the endoplasmic reticulum. The enzyme is thus viewed as a multicomponent system involving at least five polypeptides subunits (4) among which T1, T2, and T3 would represent specific transporters for Glu-6-P, phosphate, and glucose, respectively. In support of the substrate-transport model are reports on the successful purification of T3 (6) as well as cloning of a cDNA encoding a 52-kDa glucose-transport protein (GLUT7) that has been assimilated to T3 (7).

Since GLUT7 has been expressed in COS7 cells (7), a cell line that does not normally contain significant amount of Glu-6-Pase activity (8), those studies do not resolve the functional relationships between glucose transport and Glu-6-P hydrolysis. In the combined conformational flexibility-substrate transport model (9–11), Glu-6-Pase traverses the microsomal membrane as a channel-forming protein embedded within the hydrophobic matrix of the bilayer, a concept that is indeed supported by the cloned sequences of the human (1) and murine (2) genes that predict up to six transmembrane segments in the secondary structure of the enzyme. In that model, the catalytic site is assumed to be located within a water-filled proteinaceous pore accessible to the substrate from the cytoplasmic surface of the membrane (11).

In agreement with the conformational model, our recent kinetic studies using a fast sampling, rapid filtration apparatus (FSRFA, U. S. patent 07/697,769) have brought evidence for a tight-coupling between Glu-6-P transport and Glu-6-Pase activity (12) but failed to demonstrate any significant transport of D-glucose into microsomes under zero-trans uptake conditions (13). In the presence of [14C]Glu-6-P in the incubation medium, however, we also showed that tracer glucose accumulates within the intramicrosomal space against a concentration gradient (12). In the present studies, we thus report on the kinetics of glucose transport into microsomes in comparison with those of Glu-6-P hydrolysis by Glu-6-Pase. Our results demonstrate that intramicrosomal glucose accumulation is directly proportional to Glu-6-Pase activity, while glucose efflux...
may occur independent of hydrolysis, so that microsomal glucose transport appears unidirectional.

EXPERIMENTAL PROCEDURES

Microsome Purification—Liver microsomes were isolated from overnight-fastened male Wistar rats (200-250 g) as described previously (12) and resuspended at a protein concentration of 10–16 mg/ml in a 50 mM TRIS-HCl buffer (pH 7.3) containing 0.25% sucrose. Glucose dehydrogenase activity was used as an index of microsomal integrity since being fully latent in intact microsomes (13, 14), and our microsomal preparations routinely displayed 95–100% latency.

Uptake and Efflux Experiments—Tracer uptake into microsomes was determined using a FSFRA as described previously (12) except for the omission of EGTA in the incubation media, which are usually adjusted to 1 mM. For zero-trans uptake experiments, 40 μl of microsomes were injected into the incubation chamber of the FSFRA and incubated at 30 °C in the presence of 0.2-10 mM concentrations of Glu-6-P while keeping the concentration of [U-14C]Glu-6-P (specific activity, 200 mCi/mmol, ICN Biomedicals, Montreal, Canada) constant at 3–4 μCi/ml incubation medium. For uptake experiments in the presence of vanadate, microsomes were preincubated or not for 1 min at 30 °C in the presence of the vanadate concentrations shown in the legend to Fig. 3. For efflux experiments, [14C]glucose-loaded microsomes were first prepared upon preincubation for 2 min at 30 °C in the incubation chamber of the FSFRA using tracer and cold Glu-6-P concentrations as above before injection of various effectors (50 μM) into the uptake medium. In both cases, samples were automatically collected at different time intervals and washed on nitrocellulose filters before determination of radioactivity of 0.2 mM [U-14C]Glu-6-P as the reference for all concentrations (mean 3.5 ± 0.2 and 3.2 ± 0.4 μM in those experiments) (19), and where y and y0 stand for the inhibited and uninhibited rates or amplitudes, respectively, while Km is the same meaning as above and can be fixed to the values determined in the corresponding data (20).

Efflux (E) data were analyzed according to Equations 8 and 9, which assume either single or double exponential decay, respectively,

\[
E = (E_0 - E_2) e^{-\kappa t} + E_2
\]

(Eq. 8)

\[
E = (E_0 - E_2) e^{-\kappa t} + (E_1 - E_2) e^{-\kappa t} + E_2
\]

(Eq. 9)

where \( E_r \) represents the starting level while \( E_1 \) and \( E_2 \) stand for the steady-state levels of intramicrosomal tracer reached with first-order rate constants \( \kappa_1 \) and \( \kappa_2 \), respectively. The initial efflux rates (\( V_0 \)) shown in Fig. 5B were calculated from Equation 8 using Equation 10.

\[
V_0 = k_2 (E_0 - E_2)
\]

(Eq. 10)

In this paper, we have chosen the parameter \( t_{1/2} \), which represents the time at which 50% of a process has been completed, to characterize the rates of influx into, and efflux from microsomes. This parameter was calculated using Equation 11.

\[
t_{1/2} = \frac{\ln 2}{\text{first order rate constants} (\kappa_1, \kappa_2)}
\]

(Eq. 11)

All kinetic analyses were performed using the Enzfitter software (Elsevier-Biosoft) and nonlinear regression analyses to pertinent equations above were performed using the robust weighting routine in conjunction with the explicit weighting routine when appropriate. Accordingly, the errors associated with the kinetic parameters as given in the text and figures represent the standard errors of regression (S.E.R.) on these parameters.

RESULTS

Comparative Kinetics of Intramicrosomal Tracer Uptake and Glu-6-P Hydrolysis—Fig. 1 (closed symbols) extends to Glu-6-P concentrations varying up to 10 mM our former conclusion that tracer accumulation into microsomes is a biphasic process that achieves a steady-state level of uptake over a 2-min period of incubation (12). In contrast, total glucose production from Glu-6-P hydrolysis (results not shown), which is also a biphasic process characterized by an initial burst phase, reaches a steady-state rate by 10 s of incubation under similar conditions (12, 16). As shown in Fig. 2A, 1) the rapid phase in tracer uptake (open triangles) and the burst phase in total glucose production (closed squares) appear synchronous and independent of Glu-6-P concentrations in mean \( t_{1/2} \) values of 3.5 ± 0.2 and 3.2 ± 0.4 s, respectively, and 2) the slow phase in tracer uptake (closed circles) occurs during the steady-state phase in glucose production and is also insensitive to Glu-6-P concentrations (mean \( t_{1/2} \) = 46.4 ± 5.3 s).

\[
A = (A_1 - A_0)(1 - e^{-k_1 t}) + (A_2 - A_0)(1 - e^{-k_2 t}) + A_0
\]

(Eq. 2)

in which \( A_1 \) represents the background in radioactivity while \( A_2 \) and \( A_0 \) stand for the steady-state levels of tracer accumulation reached with first-order rate constants \( k_1 \) and \( k_2 \), respectively. Since \( k_1 \) is 1 order of magnitude larger than \( k_2 \) (12), the uptake time courses were first fitted over the 10–240-s time range using Equation 3.

\[
A = (A_2 - A_0)(1 - e^{-k_1 t}) + A_0
\]

(Eq. 3)

in order to determine the parameters \( A_2, A_0 \), and \( k_2 \). Those values were then used as prompted constants into Equation 2 when analyzing the whole time range. Amplitudes and initial rates of accumulation during the fast (\( AMP_1, V_{AMP_1} \)) and slow (\( AMP_2, V_{AMP_2} \)) phases were calculated as shown in Equations 4 and 5.
Influx and efflux experiments were performed as described in the text in the presence of final concentrations of 0.2 ( ● ), 0.5, 1, 2 ( ● ), 5, and 10 mM Glu-6-P ( □ ). Alternatively, 50 mM cold glucose ( ▲ ) was added under efflux conditions. Arrow indicates the time of effector additions for efflux experiments. For the sake of clarity, only three out of the six uptake curves and two out of the five efflux curves are shown with their respective regression lines. Each point represents the mean of five determinations using the same microsomal preparation. The error structure followed a proportional distribution with mean S.D. of 7.9 ± 1.3%.

The uptake time curves shown in Fig. 1 (closed symbols) clearly indicate, however, that the steady-state levels of intramicrosomal tracer accumulation are affected by unlabeled Glu-6-P concentrations. A close link between the steady-state rate of tracer Glu-6-P hydrolysis (VSS) and the amplitude of the slow phase of intramicrosomal tracer accumulation (AMP2) is indeed suggested by the results of Fig. 2B showing similar Km values for both processes (1.37 ± 0.05 and 1.22 ± 0.12 mM, respectively). Those results indicate, as also argued previously (12) but demonstrated in the companion paper (21), that glucose is the main labeled species to be found inside of the microsomes. In this respect, it is worth pointing out that we failed to demonstrate directly tracer uptake from [14C]Glu-6-P when incubated under zero-trans conditions with liver microsomes isolated from a type 1a glycogen storage disease patient (22).

Glucose Efflux from Microsomes Following Isotopic Dilution by Cold Glu-6-P—In the next series of experiments, [14C]glucose-loaded microsomes were exposed to either cold glucose or Glu-6-P. The addition of 50 (Fig. 1, open circles) or 100 mM glucose (results not shown) failed to induce glucose efflux from microsomes. In contrast, the addition of an excess cold Glu-6-P (open squares and triangles) caused a decrease in radioactivity within the vesicles, thus demonstrating that intramicrosomal glucose may exchange with cold glucose produced by Glu-6-P hydrolysis. Moreover, glucose efflux under these conditions is dose-dependent, and similar steady-state levels of intramicrosomal glucose are observed under symmetrical conditions of Glu-6-P concentrations during influx and efflux experiments. For added Glu-6-P concentrations of 0.3–1.8 mM, the efflux curves can be fitted to the single exponential decay Equation 8 only, and the corresponding t1/2 values are shown in Fig. 2A (open circles). At Glu-6-P concentrations of 4.8 and 9.8 mM, however, both fast and slow phases become apparent using Equation 9. For the former, t1/2 values of 4.6 ± 1.2 and 3.1 ± 0.6 s and amplitudes representing 18 and 26% of total efflux are observed at 4.8 and 9.8 mM Glu-6-P, respectively. For the latter, the t1/2 values are given in Fig. 2A (open circles) where it should be noted that the slow component of efflux is quite insensitive to Glu-6-P concentrations with a mean t1/2 value of 20.1 ± 2.0 s.

Effect of Vanadate on Glucose Accumulation into, and Efflux from, Microsomes—To further establish the link between intramicrosomal glucose accumulation and Glu-6-Pase activity, both influx and efflux studies were performed in the presence of sodium vanadate, a potent competitive inhibitor of Glu-6-P hydrolysis (23). First, microsomes were preincubated for 1 min in the presence of 0–100 μM vanadate and then further incubated with 0.2 mM [U-14C]glucose under zero-trans conditions (Fig. 3, closed symbols). Glucose uptake in the presence of 0.2 mM Glu-6-P alone (closed circles) could be fitted to Equation 2 with t1/2 values of 2.6 ± 0.9 and 3.1 ± 0.5 s for the fast and slow uptake phases, respectively. In the presence of vanadate (closed squares and triangles), however, the uptake data could be fitted to Equation 3 only, and Fig. 4A (closed circles) shows that the t1/2 for intramicrosomal glucose accumulation is insensitive to vanadate concentrations in the incubation medium (mean t1/2 = 32.8 ± 2.6 s). In contrast, Fig. 3 (closed squares and triangles) clearly shows that the steady-state level of intrami-
crosomal glucose accumulation is affected by vanadate concentrations. A close link between $V_{SS}$ (closed circles) and the amplitude of the slow phase of intramicrosomal tracer accumulation ($AMP_2$, open circles) is demonstrated in Fig. 4B, showing that both processes are inhibited competitively by vanadate with similar $K_v$ values ($K_v = 10.1 \pm 1.3$ and $22.2 \pm 0.8 \mu M$, respectively).

Next, $[^{14}C]$glucose-loaded microsomes were exposed to vanadate concentrations varying from 0 to 100 $\mu M$ in a 50 mM TRIS-HCl buffer (pH 7.3) containing 0.25M sucrose. As shown in Fig. 3, buffer addition alone (open circles) had no effect on the steady-state level of intramicrosomal glucose accumulation. In contrast, vanadate addition (open squares and triangles) caused glucose efflux from microsomes down to the same steady-state levels that were achieved under the symmetrical zero-trans uptake experiments. The efflux data can be fitted to Equation 8 only over the whole range of inhibitor concentrations, and Fig. 4A (open circles) demonstrates that the $t_{1/2}$ values of glucose efflux decreased from 197 ± 26 down to 47.5 ± 1.4 s for vanadate concentrations increasing from 10 up to 100 $\mu M$. The higher $t_{1/2}$ values obtained after the addition of low concentrations of vanadate (5-20 $\mu M$) may be related to the relative inaccessibility of the inhibitor to the catalytic site in intact microsomes (23). In agreement with that idea, the apparent $t_{1/2}$ for glucose accumulation into microsomes decreased from 35.2 ± 3.9 s in the absence of inhibitor down to 8.5 ± 2.2 s at 100 $\mu M$ vanadate in zero-trans uptake experiments where the preincubation step with vanadate was omitted (Fig. 4A, closed triangles). Under these conditions, however, the steady-state levels of intramicrosomal glucose accumulation and their dependence on inhibitor concentrations were similar to those presented in Fig. 4B for preincubated microsomes.

In a last series of experiments, it was observed that other classical inhibitors of Glu-6-Pase activity that act by mechanisms different from that of vanadate like 4,4'-disothiocyana
tostilbene-2,2'-disulfonic acid, NaCl, NaF, and phlorizin (19), were also able to induce glucose efflux from glucose-loaded microsomes (data not shown).

Mechanism and Kinetic Characteristics of Glucose Transport in Rat Liver Microsomes—The question as to whether glucose transport is a saturable process was investigated by measuring glucose efflux caused by the addition of a saturating concentration of 200 $\mu M$ vanadate to glucose-loaded microsomes upon 2 min of incubation in the presence of varying concentrations of Glu-6-P as in Fig. 1 (closed symbols). The efflux curves were fitted to Equation 8 with $t_{1/2}$ as shown in Fig. 5A for intramicrosomal glucose concentrations calculated from the steady-state levels of tracer accumulation and the microsomal volume. The $t_{1/2}$ values are randomly distributed between 28.7 and 45.6 s with a mean value of 37.3 ± 5.5 s. We then calculated the initial rates of glucose efflux using Equation 10, and Fig. 5B clearly shows the linear correlation between glucose efflux rates and intramicrosomal glucose concentrations with no appearance of saturation over the analyzable range. It should be noted that the slope value of 11.2 ± 0.6 pmol/s/mg of protein·mM is equivalent in microsomes to a first order rate constant of 0.0140 ± 0.00025 s⁻¹ or $t_{1/2} = 49.5 ± 8.8$ s, a value closely matching that found in Fig. 2A (closed circles) for the slow component of intramicrosomal tracer uptake.

The above results seem to indicate that glucose equilibration...
Glucose uptake into microsomes can be readily monitored in the presence of zero-trans concentrations of [14C]Glu-6-P (Fig. 1, closed symbols), and can be inhibited by vanadate (Fig. 3, closed symbols) or saturating concentrations of phlorizin (12). Similarly, glucose efflux from [14C]glucose-loaded microsomes can be demonstrated following isotopic dilution by cold Glu-6-P (Fig. 1, open symbols), inhibition of Glu-6-Pase activity by vanadate (Fig. 3, open symbols), or a series of Glu-6-Pase inhibitors acting by different mechanisms. It should be stressed, however, that zero-trans uptake of radiolabeled d-glucose could not be observed under conditions where glucose produced from Glu-6-P hydrolysis readily exchanges between the intravesicular space and the external medium (Ref. 13 and this study). Accordingly, glucose influx into microsomes appears tightly linked to Glu-6-Pase activity, while glucose efflux may occur independently of hydrolysis so that glucose transport appears unidirectional in the absence of enzyme activity.

The dose link between glucose transport and Glu-6-P hydrolysis is further supported by the observations that the steady-state levels of intramicrosomal glucose accumulation 1) follow Michaelis-Menten kinetics relative to outside Glu-6-P concentrations with a $K_m$ value similar to that of total glucose production via Glu-6-P hydrolysis (Fig. 2B) and 2) appear to be inhibited competitively relative to outside vanadate concentrations with a $K_i$ value in the same range as that obtained for inhibition of Glu-6-Pase activity (Fig. 4B). Accordingly, glucose accumulation from [U-14C]Glu-6-P is directly proportional to Glu-6-Pase activity and limited by the maximum rate of the enzyme.

The impermeability of microsomes to glucose in the inward direction is further demonstrated by the absence of isotopic exchange between intra- and extramicrosomal glucose following addition of an excess cold glucose to [14C]glucose-loaded microsomes. Under similar conditions, however, addition of an excess cold Glu-6-P does result in glucose exchange with the intravesicular space and leads to faster glucose efflux (Fig. 2A, open circles, mean $t_{1/2} = 20.1 \pm 2.0$ s) than observed upon addition of 100 $\mu$M vanadate (Fig. 4A, open circles, $t_{1/2} = 47.5 \pm 1.4$ s). On the other hand, a $t_{1/2}$ value in the range of that found for influx (Fig. 2A, closed circles, $t_{1/2} = 46.4 \pm 5.3$ s) is observed for efflux (Fig. 5A, $t_{1/2} = 37.3 \pm 5.5$ s) when initiated by the addition of a saturating concentration of vanadate to [14C]glucose-loaded microsomes. To understand these results, one should remember that, contrary to the situation with vanadate where efflux occurs at constant specific radioactivity of inside glucose and outside Glu-6-P, tracer glucose efflux elicted by the addition of cold Glu-6-P takes place under conditions of net glucose influx, i.e. under conditions where the specific radioactivity of the intramicrosomal glucose pool is continuously changing with time. What is observed, then, is an apparent rate of tracer efflux, and it can be predicted that its value would be twice as fast as that recorded under net efflux conditions when assuming that the same process of diffusion is involved for both tracer efflux and cold glucose influx. Indeed, the results of Figs. 2A (open circles, no change in the $t_{1/2}$ for efflux at increasing Glu-6-P concentrations) and 5B (no saturation of the efflux rate over the analyzable range of intramicrosomal glucose concentrations) do support such an interpretation.

The conclusions that microsomal glucose transport is unidirectional and occurs through diffusion deserve some comments. First, unidirectionality of transport may only be apparent since, as argued recently by Burchell (8), "direct measurement of labeled glucose uptake into microsomes is difficult because the transport is very rapid and relatively low number of counts are taken up into the microsomal lumen." We do think, how-

![Image](64x388 to 278x745)

**Fig. 5.** Efflux kinetics as a function of intramicrosomal glucose concentrations. As in Fig. 1 (closed symbols) for influx experiments, microsomes were preincubated for 2 min at various [14C]Glu-6-P concentrations before the addition of 200 $\mu$M vanadate. The time courses of efflux were monitored for an additional 2 min. The intramicrosomal glucose concentrations, and both the $t_{1/2}$ for efflux (A) and the initial rates of efflux (B) were determined as described in the text. Lines shown correspond to the linear regression analysis of the data points ± S.E.R.
ever, that zero-trans glucose transport, if occurring, should be measurable in that preparation; 1) glucose uptake can be readily measured in other vesicle systems with similarly small intravesicular volumes (17); 2) the problem of low number of counts can be partly solved by using pure tracer concentrations of glucose with high specific activity (18) (the sensitivity of the transport assay in terms of measurable cpm's would be maximum under those conditions, see Equation 6 when S = 0); and 3) the rapidity of the uptake process is readily overcome in our laboratory when using the FSRFA. In agreement with those statements, it is worth emphasizing that zero-trans uptake of inorganic phosphate could be successfully measured in both rat and human liver microsomes (22). Moreover, since phosphate was taken up into an equivalent microsomal space of 1.2 μL/mg of protein (22), thus closely matching that of 0.8 μL/mg of protein determined in previous studies using 3H2O (12), it can be concluded further that the use of the FSRFA does not damage a major fraction of the vesicles such as to preclude significant zero-trans uptake measurements. Accordingly, our failure to detect glucose uptake under similar and appropriate experimental conditions can thus be taken as evidence that glucose does not enter into a measurable intravesicular space at any significant rate. We do not rule out, however, the possibility that glucose may permeate the endoplasmic reticulum membrane through passive diffusion with extremely low rate constant. Next, diffusion may only be apparent since, in the low range of substrate concentrations, a low affinity carrier or channel may not show saturation kinetics (the apparent diffusion constant in that case is equal to the Vmax/Km ratio of the transport protein, see Equation 6 with S and T ≪ Km). Unfortunately, due to their low glucose permeability, it is not possible to passively load microsomes in a reliable way at fixed glucose concentrations, and thus to extend the range of sugar concentrations over which saturation kinetics (or the lack thereof) might be observed in plots like those shown in Fig. 5B. Accordingly, the upper range of analyzable intravesicular glucose concentrations is fixed to 15–20 mM when active loading from [14C]Glu-6-P is used, a value dictated by the Vmax of Glu-6-P hydrolysis by Glu-6-Pase. In that respect, the slight deviation from linearity observed at 20 mM inside glucose in the plot of Fig. 5B should not be taken as evidence for the beginning of the development of a hyperbolic relationship because the low signal to noise ratio that is achieved at close to complete saturation of the enzyme does not allow for a precise estimate of the intramicrosomal glucose concentration. Moreover, if one assumes that a transport protein like GLUT7 is present within the microsomal membrane, we may expect 1) inhibition of glucose efflux from microsomes by phloretin (7), 2) accelerated efflux of glucose from [14C]glucose-loaded microsomes following addition of an excess cold glucose to the incubation medium, 3) zero-trans uptake of tracer glucose with t1/2 in the range of 30–50 s since the same Vmax/Km ratios should be observed under influx and efflux conditions independent of whether the transporter is symmetrical or not due to the law of microscopic reversibility (25), and 4) zero-trans uptake of tracer glucose with overshoot phenomenon (25) in microsomes loaded with cold glucose. Since none of these expectations could be demonstrated in our experiments, we must conclude that glucose transport is indeed unidirectional and may not involve GLUT7. Should a specific glucose transport protein (T3) be present in native liver microsomes, however, we do state that its kinetic properties are different from those demonstrated for GLUT7 in COS7 cells (7), maybe due to a close association with a multicomponent enzyme complex (4, 6, 8). In any case, it should be stressed that the model proposed in the companion paper (21) requires the presence of neither GLUT7 nor any other glucose transport protein but for Glu-6-Pase in order to explain the steady-state kinetics of Glu-6-P hydrolysis and glucose exchange through the microsomal membrane.

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