A Test for Passive Absorption of Glucose in Yellow-Rumped Warblers and Its Ecological Implications

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ABSTRACT

In an earlier study, we found that yellow-rumped warblers had in vitro active uptake rates of D-glucose that were only a few percent of the glucose absorption rate achieved at the whole-animal level. Here we used a pharmacokinetic technique to test whether a substantial amount of sugar can be absorbed passively. We used yellow-rumped warblers (*Dendroica coronata*), known for their seasonal frugivory, freely feeding on a synthetic mash formulated with naturally occurring concentrations of D-glucose. Birds absorbed 89.8% ± 1.0% (SE) of the D-glucose in the mash. When fed the same mash with trace-labeled ^{3}H L-glucose, the stereoisomer that does not interact with the intestinal Na^+-glucose cotransporter, ^{3}H appeared in plasma, an indication that this stereoisomer of glucose was absorbed. We used ^{3}H levels in plasma and excreta in a pharmacokinetic model to calculate L-glucose extraction efficiency (i.e., the percent absorbed). Calculated mean extraction efficiency for the passively absorbed L-glucose averaged 91% ± 23%. Our finding of considerable passive absorption reconciles the in vitro and in vivo results for D-glucose absorption and is in concert with results from five other avian species. The passive pathway appears to provide birds with an absorptive process that can respond quickly to changing luminal concentration and that is energetically inexpensive to maintain and modulate in real time but that may bear a cost. Less discriminate passive absorption might increase vulnerability to toxins and thus constrain foraging behavior and limit the breadth of the dietary niche.

Introduction

The relative contribution to total in vivo glucose transport of active versus passive transport has been a vexing problem for digestive physiologists for years and is currently hotly debated (Diamond 1991; Pappenheimer 1993). Our interest in the problem arose from findings that in several avian species low active D-glucose transport was measured in vitro, but a higher ability to absorb D-glucose was measured in vivo. In a companion study to this one, we found that yellow-rumped warblers (*Dendroica coronata*), well known to switch seasonally between insects and fruit (review in Afik et al. [1995]), had in vitro active uptake rates of D-glucose only a few percent of what they could apparently achieve at the whole-animal level and that were not up-regulated by high dietary D-glucose (Afik et al. 1997). It is difficult to rule out a technical explanation for this—that the in vitro technique grossly underestimates active transport in vivo—though there are several reasons for thinking that this is not the case (Afik et al. 1997) . Therefore, we sought independent evidence for the alternative explanation—that substantial passive absorption of glucose occurs.

Determining the relative contribution of active versus passive transport of sugars has important implications for understanding and predicting features of avian feeding ecology. For example, it has been argued that, because foods may contain toxins, there would have been selection against reliance on passive absorption in favor of the specificity of absorption via specific transport proteins in the intestinal brush border (Diamond 1991). Under this scenario, we might expect that a primarily insectivorous bird that lacks large numbers of the specific intestinal D-glucose transport proteins (i.e., active transport) would forage under a constraint; it would have a low ability to absorb the D-glucose in sugar-rich foods such as fruit or nectar or excretions of sap-drinking insects (honeydew). Foraging on poorly absorbed substrates not only wastes time but can lead to life-threatening osmotic diarrhea as well (Brugger and Nelms 1991). This constraint might be relaxed if the species' intestinal D-glucose transporter had its activity reversibly and specifically induced by dietary D-glucose. Under the alternative scenario of reliance on passive absorption, the species might forage under a different constraint: the need to avoid overingestion of any fruit toxins that are absorbed passively along with sugar, such as low molecular weight, water soluble alkaloids, and simple phenolics (Goldstein and Swain 1963; Janzen 1983; Ballington et al. 1988; Harborne 1988; Cipollini and Stiles 1992).

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As a test for passive absorption, we applied a pharmacokinetic technique to measure in vivo absorption of L-glucose, the stereoisomer that does not interact with the intestinal Na^+-glucose cotransporter (Karasov and Cork 1994). Also, because we did not have an accurate measure of D-glucose absorption rate in vivo in our previous study, we measured it here. Yellow-rumped warblers are a good species for studying this issue because in the wild they do ingest foods rich in simple carbohydrates. Yellow-rumped warblers feed primarily on arthropods during the summer but include a large proportion of fruit and other sugar-rich foods in their diet such as sap, honeydew, and nectar during migration and in winter (review in Afik et al. [1995]).

Material and Methods

Birds and Their Maintenance

Yellow-rumped warblers were caught in mist nets during fall migration in Chippewa Falls, Wisconsin (45°00′ N, 91°30′ W), and transferred to our laboratory in Madison, where they were banded and housed in individual stainless-steel cages (60 × 45 × 33 cm) under constant light cycle and temperature (21°C; 12L : 12D). We lost 15% of our birds in the first 48 h, probably due to capture-related stress, but had no mortality later on. We maintained the birds on a synthetic banana-based maintenance diet (Denslow et al. 1987) supplemented with four to five mealworms or waxworms and water ad lib. daily.

Three trials were performed. Trial 1 measured extraction of D-glucose from mash diet, and trials 2 and 3 measured extraction of L-glucose. At least 3 d before a trial, we started feeding the birds with a mash with a D-glucose content of 61.4%–65.3% of dry mass. We used this new diet instead of the banana-based diet to ensure that D-glucose was the only available sugar. The mash for trial 1 was prepared by mixing 330 g water with 24 g D-glucose, 8.25 g soy protein, 3 g agar, 2.31 g vegetable oil, and 0.5 g each of sodium chloride, di-calcium phosphate, and a vitamin and mineral mixture (Chirp vitamin, minerals, and protein supplement for birds, Lambert Kay, Cranbury, N.J.). The diet for trials 2 and 3 differed slightly; it was prepared by boiling 330 g water with 4.0 g agar for 10 min and then mixing 39.0 g D-glucose, 6.0 g casein, 2.25 g of an amino acid mixture (Murphy and King 1982, Table 2), 1.0 g vitamin and mineral mixture, 3.5 g salt mixture (Briggs Salt Mixture, ICN Biochemicals), and 4.0 g vegetable oil. The sugar contents of these wet mash diets (7.2%–10%) are within the range reported for natural fruits (6%–25%; White and Stiles 1985). The birds maintained constant mass on these diets for months when it was provided as the maintenance diet.

One day before a trial, each bird was moved into a stainless-steel cage (60 × 45 × 33 cm) similar to its regular cage but whose front wall was clear Plexiglas. The inner walls of the cage were covered with Plexiglas to prevent the birds from perching and defecating on the side bars. One available perch was hung from the center of the cage's ceiling. A dish full of the bird's food was placed in a holder mounted to the wall of the cage. A roll of continuous plastic-coated paper (S/P Absorbent Paper Baxter Cat L5616-1), with the plastic facing up, was installed behind each cage, so that the sheet could be pulled beneath through the cage's floor. Two such cages were housed next to each other inside a frame covered on the sides and top with nontransparent plastic. The front wall of the frame was clear Plexiglas onto which we applied a sheet of Mylar. Two fluorescent lights were placed on top of the cage, and when lights were dimmed in the animal room, the bird saw its reflection but could not see us as we looked in. With these cages we could observe when a bird ate, and we could collect clean excreta with little or no disturbance to the bird, whereas the presence of a visible observer in front of its regular cage usually caused excessive agitation and gut emptying.

Trial 1: Measurement of D-Glucose Absorption in Vivo

Feeding rate over 4 h was measured by disappearance of food, with correction for the food's water content. At time zero, birds were force-fed a bolus of the mash containing 0.5 μCi ^{14}C D-glucose (NEN Research Products, DuPont, Wilmington, Del.) and an inert marker, 2 μCi [1,2-^{3}H] polyethylene glycol (PEG; mol wt = 4,000; NEN). Excreta were collected for 12 h, during which 95% of the nonabsorbable marker PEG was excreted (Karasov and Dykstra 1991; D. Afik, unpublished data). Samples of food and excreta were counted by liquid scintillation to determine the disintegrations per minute (dpm) for each tracer (Afik and Karasov 1995). Extraction efficiency (E) for D-glucose in the mash was calculated by the inert indicator ratio technique (Karasov et al. 1986) using the following equation: $E = 100 - 100[(\text{dpm}_{\text{im-food}}/\text{dpm}_{\text{n-food}}) \times (\text{dpm}_{\text{n-excreta}}/\text{dpm}_{\text{im-excreta}})]$, where $\text{dpm}_{\text{im-food}}$ and $\text{dpm}_{\text{im-excreta}}$ are disintegrations per minute of the inert marker in the food and excreta, respectively, and $\text{dpm}_{\text{n-food}}$ and $\text{dpm}_{\text{n-excreta}}$ are disintegrations per minute of the nutrient in the food and excreta, respectively.

Trials 2 and 3: Measurement of L-Glucose Absorption in Vivo

We used a pharmacokinetic technique that involves feeding and injecting radiolabeled L-glucose and then sampling blood (Tuey 1980; Karasov and Cork 1994). The L-glucose is absorbed passively but is not metabolized and is entirely excreted (Karasov and Cork 1994). Extraction efficiency is calculated as: $E = 100(L \times k_{el} \times S)/I$, where L is the level of labeled L-glucose in plasma (dpm g^{-1} plasma), k_{el} is the elimination constant for removal of L-glucose from plasma and its excretion in urine (min^{-1}), S is the distribution space of L-glucose in plasma

(g plasma), and I is the ingestion rate of labeled L-glucose (dpm min^{-1}).

These parameters were established in two trials. In another study using this pharmacokinetic technique with a larger avian species (Karasov and Cork 1994), these parameters were all measured in one trial by repetitive blood sampling. Because yellow-rumped warblers were too small to permit this (12 g), we determined the distribution space of L-glucose in plasma in trial 2 from blood samples and then determined the other parameters in trial 3 from excreta and blood samples.

To measure the distribution space of L-glucose in plasma in trial 2, and to make a qualitative check for absorption of labeled L-glucose, we injected 16 warblers at noon in the pectoralis with ^{14}C L-glucose (1.2 μCi in 30 μL of 1% NaCl; American Radiolabel Chemicals). Ten of these birds had been eating mash with ^{3}H L-glucose (1 μCi g^{-1} wet mash; NEN Research Products, DuPont, Wilmington, Del.) for the previous 5 h and continued to eat it after injection. At intervals separated by at least 15 min, we removed each bird from its cage and took 30–40 μL of blood from the brachial vein (no more than two samples per bird). By sampling from different birds at different times, we obtained at least three replicates each for 20, 30, 40, 65, and 80 min postinjection. Twenty minutes is time enough for distribution of isotope throughout the space (Karasov and Cork 1994). Blood was cooled to 4°C and centrifuged for 5 min at 4,000 rpm for separation of plasma. Plasma samples were weighed (10–20 mg) and counted by liquid scintillation with correction for variable quenching and spill of each isotope into the channel of the other isotope. Plasma activity of each bird was normalized to the bird's dose, determined by weighing the syringe prior to and after injection. All the data were fitted (nonlinear curve fitting; Gauss-Newton method; SYSTAT, Wilkinson 1992) to the following model: plasma activity $= Ae^{(k_{el} \times t)}$, where A is the intercept, k_{el} is the elimination constant of ^{14}C L-glucose, and t is time since injection. The distribution space of L-glucose in plasma is then the inverse of A. We used nonlinear curve fitting for parameter derivation because the variance of the dependent variables would be related to the independent variables (Motulsky and Ransnas 1987), increasing with time due to interindividual differences in excretion rate.

In trial 3, six birds were placed in the observation cages 1 d prior to the test day. At 0800 hours on the test day, birds were provided with unlabeled mash. At 1200 hours, ^{14}C L-glucose was injected into the pectoralis, and excreta were collected every 15 min during the subsequent 240 min. Birds were provided mash with ^{3}H L-glucose after injection. We established the level of L-glucose in plasma by taking a blood sample from the brachial vein of each bird at approximately 1600 hours. Plasma samples were weighed and counted by liquid scintillation. Excreta were weighed, dissolved in 5 mL water, refrigerated, and remixed daily for at least 3 d to ensure solubilization of label. Then, 1-mL aliquots were counted by liquid scintillation. Counts of both plasma and excreta were corrected for variable quenching and spill of isotope into the channel of the other isotope. The elimination constant for removal of L-glucose for each individual was calculated from the rate of decline of specific activity in excreta, as described and validated elsewhere (Karasov and Cork 1994). To estimate the ingestion rate of labeled L-glucose, we first determined for each bird its ratio of mash consumed (g) to mass excreted (g) (2.31 ± 0.31, $n = 6$) and then multiplied that ratio by the bird's excreta mass for the 90 min before blood sampling. This procedure was necessary because feeding was depressed when birds were first given radiolabeled food 4 h earlier, just after being injected. Because the L-glucose activity in the blood sample taken at 1600 hours corresponds to concurrent rates of L-glucose intake and excretion, use of the lower intake rate calculated over the entire 4-h period, compared with the higher intake during the last 90 min alone, would have led to overestimation of absorptive efficiency. Activity in food was determined as for excreta.

This in vivo technique assumes that the excretion of L-glucose can be approximated by single pool kinetics. We concluded that this was the case based on inspection of plasma and excreta decay curves following injection of labeled L-glucose (below). The technique also assumes that absorbed L-glucose is not metabolized but is entirely excreted. We found in an earlier study with another avian species that 94% of injected L-[^{3}H]glucose was recovered (Karasov and Cork 1994).

We used thin-layer chromatography (Lato et al. 1968) to establish that in yellow-rumped warblers most ^{3}H in plasma was absorbed as L-glucose. On two occasions a year after the original in vivo absorption study, three yellow-rumped warblers, fed food and water ad lib., were gavaged with 60 μL of 175 mmol L^{-1} D-glucose solution containing 12 μCi ^{3}H L-glucose. Blood was drawn 30 min later. Samples (2 μL) of bird plasma and also dilutions of the gavage solution alone, or mixed 1 : 2 (by mass) with plasma from unlabeled birds, were counted directly by liquid scintillation (EcoLume cocktail) and also spotted onto plates (Whatman PE SIL G/UV silica gel with fluorescent indicator) that were then placed in solvent for 5 h (see Lato et al. [1968] for more details). When sprayed with methanol with 20% sulfuric acid and developed with a heat gun, the naturally occurring plasma D-glucose stained darkly. We assumed that L- and D-glucose have similar rates of movement of solute and defined the L-glucose band according to the location of nonlabeled D-glucose spotted onto plates run simultaneously. That band, plus four similar-sized bands both below and above it incorporating the full length from starting point to solvent front, were cut, placed into scintillation vials with EcoLume cocktail, and counted by liquid scintillation once silica material had visibly dissolved off the gel backing. In all cases, most of the ^{3}H activity was in the glucose band: for experimental birds, 95% ± 1% ($n = 3$ birds, measured

twice each and averaged); for gavage solution, 94% ± 1% (n = 7); for gavage solution mixed with plasma, 93% ± 1% (n = 5). The counts recovered on the plates were generally about half that of similar sample volumes counted directly; for gavage solution, 56% ± 4% (n = 7); for gavage solution mixed with plasma, 48% ± 9% (n = 5); and for plasma from experimental birds, 53% ± 1% (n = 3). Recovery may have been low due to binding of label to the thin-layer chromatography plate or because we did not scrape the plates; plates simply placed into scintillation cocktail immediately after labeled solution was applied (i.e., not placed into solvent for 5 h and later developed) had 48% ± 3% (n = 6) of the counts of similar volumes of solution counted directly. Considering the similar recovery of radiolabel in the glucose band for both the gavage solution and bird plasma, we concluded that the tritium in bird plasma was absorbed from the gavage solution attached to L-glucose.

Results throughout are given as means ± SE.

Results

Yellow-rumped warblers absorbed 89.8% ± 1.0% (n = 6) of the D-glucose in the mash. This agrees well with our previous estimate of 88% absorption of radiolabeled D-glucose for yellow-rumped warblers eating banana mash (Afik and Karasov 1995). It also agrees with the finding that D-glucose absorption in fruit eaters (range 73%–92%; Martinez del Rio et al. 1989; Karasov and Levey 1990) tends to be lower than in nectarivores (range 97%–99%; Karasov 1990; Karasov and Cork 1994).

For the ^{14}C L-glucose that was injected, the semilog plot of activity in plasma versus time was approximately linear (r^2 = 0.93, $P < 0.0001$; Fig. 1*A*), as were the plots for activity in excreta (Fig. 2*A*). This implies single-compartment kinetics. A two compartment model did not significantly improve the fit (F = 0.0, P = 1.0; Motulsky and Ransnas 1987). The L-glucose distribution space was 3.3 ± 0.4 g plasma, corresponding to 25% of average body mass (13.41 ± 1.06 g, n = 16). This agrees well with estimates of the distribution space in rainbow lorikeets (23% of body mass; Karasov and Cork 1994), cedar waxwings (24%; D. Levey, personal communication), northern bobwhite quail (22%; Levey and Cipollini 1996), and house sparrows (24%; Caviedes-Vidal and Karasov 1996). Hence, in trial 3 we used an estimate of 25% of body mass for the distribution space of L-glucose in plasma of each individual.

L-glucose that was ingested appeared in plasma (Fig. 1*B*), a clear indication that this stereoisomer of glucose was absorbed. We used the blood sample of each bird in trial 3 to quantify the efficiency of absorption (Table 1). The corresponding value for the elimination constant for removal of L-glucose was determined for each individual from its excretion curve of injected ^{14}C L-glucose (Fig. 2*A*; Table 1). Excreta also contained ^{3}H L-glucose (Fig. 2*B*) that was either not absorbed or was absorbed and subsequently excreted in urine. The ^{3}H L-glucose first

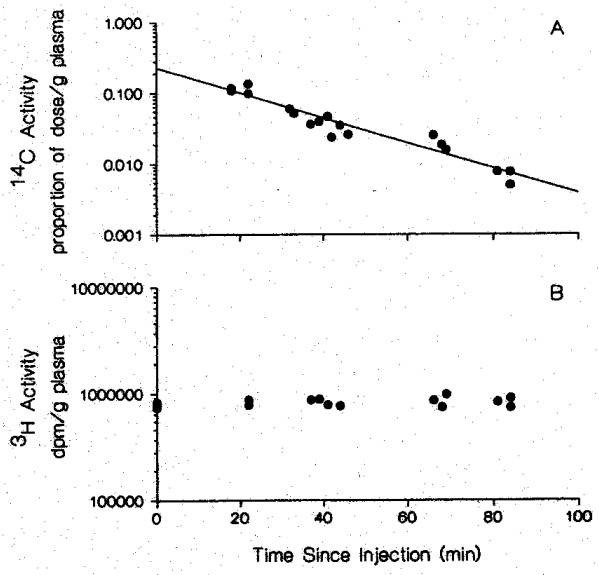

Figure 1. Specific activity in plasma of radiolabeled L-glucose that was injected or fed. *A*, Specific activity above background of ^{14}C L-glucose in plasma samples as a function of time since injection of ^{14}C L-glucose in trial 2. The abscissa is minutes, and the ordinate is ln(proportion of dose g^{-1} plasma). The linear relation for injected ^{14}C L-glucose implies that injected L-glucose was excreted with approximately single-compartment kinetics. *B*, Specific activity above background of ^{3}H L-glucose in plasma samples of the birds in *A* that were eating a diet containing ^{3}H L-glucose.

appeared 43 ± 5 min (n = 6) after ^{3}H L-glucose-containing food was first consumed and reached a plateau value 73 ± 8 min after first consumption (Fig. 2*B*). We used the feeding rate over the 90 min prior to blood sampling when birds were undisturbed to estimate the ingestion rate of ^{3}H L-glucose (Table 1). Our use of the higher feeding rate in the 90 min before blood sampling provides the most conservative estimate of absorptive efficiency. The calculated extraction efficiency for ingested L-glucose was 91% ± 23% (n = 6; Table 1).

Discussion

Based on the yellow-rumped warbler's feeding rate (22 mg wet mass min^{-1}; Table 1), D-glucose absorptive efficiency (89.8%), and diet D-glucose content (10% of wet mass), its calculated rate of D-glucose absorption was 2 mg min^{-1}, or 11 μmol min^{-1}. Our previous in vitro–based estimate of the maximal absorptive capacity of the yellow-rumped warbler's small intestine for D-glucose by active transport was no more than 0.18 μmol min^{-1} (Afik et al. 1997), only 1.6% of that measured at the whole-animal level. Our finding here that L-glucose, the stereoisomer that does not interact with the intestinal brush border Na^+-coupled glucose transporter, was almost entirely absorbed bears out our initial prediction that passive absorption must be important. Near complete absorption of ingested L-glucose is also found in nectarivorous rainbow lorikeets

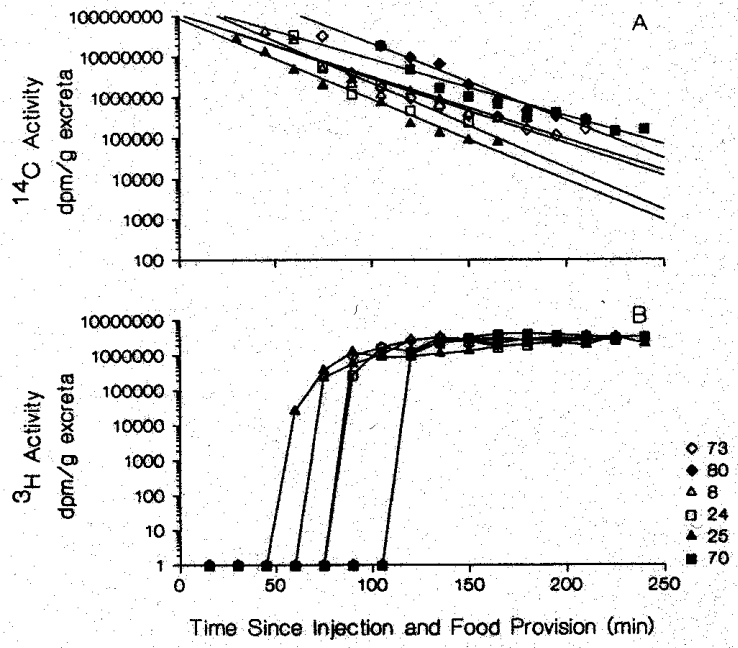

Figure 2. Specific activity in excreta of radiolabeled L-glucose that was injected or fed. *A*, Specific activity above background of ^{14}C L-glucose in excreta samples as a function of time since birds were injected with ^{14}C L-glucose and provided with food containing ^{3}H L-glucose in trial 3. Each yellow-rumped warbler is represented by a different symbol. The lines in *A* are the least squares linear fit to the marker in the excreta samples of each individual. *B*, Specific activity above background of ^{3}H L-glucose in excreta samples as a function of time since birds in *A* were injected with ^{14}C L-glucose and provided with food containing ^{3}H L-glucose in trial 3. The excreta of each bird was initially at background (hence, value set at 1).

(80%; Karasov and Cork 1994), granivorous northern bobwhite quail (92%; Levey and Cipollini 1996), house sparrows (82%; Caviedes-Vidal and Karasov 1996), and frugivorous cedar waxwings (79%; D. Levey, personal communication). The similarity of this finding in birds with diverse diet and taxonomic associations suggests a general phenomenon in birds.

The measurement of L-glucose absorption and its extension to conclusions about D-glucose passive absorption rests on several assumptions. We have assumed that the L-glucose absorption measured in vivo is entirely passive and can be equated with passive D-glucose absorption. Several studies indicate that there is no carrier for L-glucose because its uptake is not self-inhibitable. In rainbow lorikeets, brush border L-glucose uptake is not influenced by D-glucose in the bulk solution (Karasov and Cork 1994), and uptake of tracer L-glucose is not influenced by cold L-glucose in bulk solution, at least in mammals (Thomson et al. 1982; Meddings and Westergaard 1989). Because of this, our finding of substantial L-glucose absorption using tracer L-glucose should hold whether or not there is unlabeled L-glucose in the intestinal lumen or different levels of D-glucose in the lumen. Furthermore, the intestinal passive permeability coefficient of L-glucose has been found to be identical to that for D-glucose in a number of mammalian species studied in vivo (Meddings and Westergaard 1989) and in vitro (Thomson et al. 1982). Under certain conditions, in vivo D-glucose passive absorption can exceed that of L-glucose—for example, when diffusive flux is small relative to convective flux (Karasov and Cork 1994). Our study was not designed to distinguish between these modes of passive absorption, but it seems reasonable to conclude that the passive absorption of D-glucose in vivo could at least equal in magnitude that of L-glucose.

The pharmacokinetic method also assumes that the labeled L-glucose is not metabolized and is entirely excreted. No metabolism of L-glucose is observed in rainbow lorikeets (Karasov and Cork 1994) or house sparrows (Caviedes-Vidal and Karasov 1996), and in lorikeets the labeled L-glucose is entirely excreted. Our thin-layer chromatography results indicated that all of the label (^{3}H) in plasma was attached to L-glucose, from which we conclude that the L-glucose in plasma was absorbed as L-glucose. Conceivably, the label came to be associated with plasma glucose by a more circuitous route. Perhaps gut microbes (luminal or adherent) absorbed the labeled L-glucose and fermented it, yielding either labeled short-chain fatty acids or labeled H_2 gas that were absorbed across the intestine. In this case, the label on plasma glucose might be attributed to hepatic metabolism of the short-chain fatty acids or to highly reactive H_2. We consider this scenario unlikely because L-glucose was not actively transported into the microbes that have been studied so far (Castille and Lawrence 1979; Walmsley et al. 1994; Mendz et al. 1995; Yoshioka et al. 1996) and because mixed populations of gut microbes do not ferment L-glucose and synthesize short-chain fatty acids from it when provided as a substrate (Mortensen et al. 1988). Thus, the available

Table 1: Parameters to determine passive absorption of L-glucose by yellow-rumped warblers in vivo

Parameter	Value
Body mass (g)	13.2 ± .6
Food consumption:	
mg wet weight min^{-1}	21.8 ± 3.6
dpm min^{-1}	1.337 ± .22 × 10^5
Steady-state plasma L-[^{3}H]glucose (dpm g^{-1})	1.253 ± .351 × 10^6
L-glucose distribution space (g plasma)	3.3 ± .1
Elimination constant (min^{-1})	.0291 ± .0023
Calculated L-[^{3}H]glucose extraction efficiency (%)	91 ± 23

Note. Values are means ± SE of six birds. Birds were eating a formulated diet containing tracer L-[^{3}H]glucose.

evidence suggests that L-glucose is rather metabolically inert in microbes, as it is in vertebrates (Russell and Young 1990). Nonetheless, the possible involvement of microbes in the apparent absorption of labeled L-glucose could be tested by measuring the absorption in birds after suppression of gut microbes with antibiotics.

The estimate of passive absorption in this study was more variable than in the other species (SD = 0.56 vs. <0.24 in the other studies). Parameter estimation in yellow-rumped warblers was complicated in two ways. First, the birds were too small for repetitive blood sampling, and therefore not all parameters could be measured simultaneously. We think that our compromise solution, determining L-glucose distribution space by pooling blood samples in one experiment, and estimating all other parameters in a second, introduced only small errors. It seems far less likely that the distribution space, a body compartment, would vary greatly among individuals, as can rates of ingestion and excretion.

The second complication was that the birds had a lower feeding rate immediately following injection than they did several hours later. The kinetic model assumes that the plasma level of L-glucose is determined by steady-state rates of intake and excretion. Whereas studies in other avian species may have achieved this (e.g., Karasov and Cork 1994), we cannot be certain of this for the yellow-rumped warblers during the 1–2 h prior to blood sampling. We focus on this period because it approximates three to four half-lives for L-glucose (i.e., one half-life = 24 min), a period over which to expect good correspondence among the ingestion rate of labeled L-glucose, the elimination constant for removal of L-glucose, and the level of L-glucose in plasma. We suspect that the variability in our estimation of absorptive efficiency relates to this technical problem. Despite this, we consider our result certainly indicative of a substantial passive pathway for glucose.

The agreement between our parameter estimates and those of other species gives us additional confidence in our conclusions. The L-glucose distribution space was within a few percent of that observed in other species (as discussed above). Elimination constants, which should scale with mass$^{-1/4}$ (Calder 1984), ranged from 0.033 in 24-g house sparrows (Caviedes-Vidal and Karasov 1996) to 0.023 in 177-g northern bobwhites (Levey and Cipollini 1996), which bracket the elimination constant for removal of L-glucose for yellow-rumped warblers. Thus, our conclusion derived from the pharmacokinetic model of substantial passive glucose absorption in yellow-rumped warblers seems robust.

It has been suggested (Pappenheimer 1993) that passive absorption may confer a selective advantage because it requires little energy and provides a mechanism whereby rate of absorption is matched to rate of hydrolysis. Possibly, if some birds rely on passive glucose absorption, then there has been little natural selection for high glucose active transport capacity or for the ability to modulate glucose active transport, as suggested previously for modulation of active vitamin transport (Stein and Diamond 1989). This scenario could explain why measurements of mediated glucose uptake in many avian species tend to fall below measurements of total glucose absorption in vivo (Karasov and Cork 1994; Caviedes-Vidal and Karasov 1996; Karasov et al. 1996; this study) and why mediated glucose absorption is not modulated in relation to dietary carbohydrate level in American robins (Levey and Karasov 1992), northern bobwhites (Karasov et al. 1996), house sparrows (Caviedes-Vidal and Karasov 1996), or yellow-rumped warblers (Afik et al. 1997).

Arguably, the opportunistic feeding behavior of many birds may require a quickly responding digestive system, the absorptive process of which is energetically inexpensive to maintain and modulate in real time (i.e., by the concentration of nutrients in a meal). While passive absorption appears to provide these advantages, it does not come without certain other costs. A high intestinal permeability, permitting passive absorption, might be less selective than a carrier-mediated system. Evidence is accumulating that in some vertebrates other small to medium-sized hydrophilic solutes permeate the small intestine in substantial amounts by a passive route. For example, in rats, creatinine and a lipid-insoluble octapeptide are 50%–60% absorbed and then excreted in urine intact (Pappenheimer et al. 1994), and mannitol, PEG 4,000 (Ma et al. 1993), and insulin (Ma et al. 1995) are absorbed largely via a paracellular route. Less discriminant absorption of lumen contents might permit toxins to be absorbed from plant and animal material. This vulnerability to toxins could be an important ecological driving force, constraining exploratory behavior and limiting the breath of the dietary niche.

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