JOURNAL OF BACTERIOLOGY, Sept., 1966
Vol. 92, No. 3

Glucose Effect and the Galactose Enzymes of *Escherichia coli*: Correlation Between Glucose Inhibition of Induction and Inducer Transport

SANKAR ADHYA AND HARRISON ECHOLS
Department of Biochemistry, University of Wisconsin, Madison, Wisconsin

Received for publication 28 March 1966

ABSTRACT

ADHYA, SANKAR (University of Wisconsin, Madison), AND HARRISON ECHOLS. Glucose effect and the galactose enzymes of *Escherichia coli*: correlation between glucose inhibition of induction and inducer transport. J. Bacteriol. **92**:601–608. 1966. —The inhibitory effect of glucose on the induction of the enzymes required for galactose utilization ("glucose effect") was studied in *Escherichia coli*. Experiments on the uptake into the cell of labeled inducers (D-galactose-C^{14} and D-fucose-H^3) pointed to inhibition at the level of inducer transport as the possible primary mechanism of the glucose effect in the case of the *gal* enzymes. This interpretation was supported by the finding that a mutant constitutive for the *lac* enzymes was resistant to glucose inhibition of galactose induction of the *gal* enzymes; the mutant had acquired a glucose-resistant alternative transport mechanism for galactose via the constitutively synthesized galactoside permease. Further support for the transport inhibition model was provided by the finding that glucose did not substantially inhibit induction of the *gal* enzymes when glucose and galactose were produced intracellularly by β-galactosidase hydrolysis of lactose, even if excess glucose was added. The inducer uptake experiments also showed that D-galactose and D-fucose probably enter the cell via different transport systems, although uptake of both compounds was inhibited by glucose.

Monod (18) discovered that the growth of wild-type *Escherichia coli* on a minimal medium containing glucose and one of a number of other sugars followed a two-step pattern (diauxic growth), in which the utilization of the second sugar did not begin until after the supply of glucose had been exhausted and after a lag period of typically about 1 hr had elapsed. The lag period corresponds to the time required to produce induced levels of enzymes needed for utilization of the second sugar; these enzymes are not present in sufficient amount so long as glucose is present (19). This phenomenon of specific inhibition by glucose of inducible enzyme formation, observed also in the case of some inducible degradative enzymes other than those involved in sugar utilization, has become known as the "glucose effect."

A number of hypotheses have been proposed in recent years to explain the glucose effect; these were reviewed by Magasanik (16). Magasanik favored the hypothesis that glucose, because it is catabolized faster than other substrates, produces higher levels of metabolic intermediates, one or more of which then act as a repressor or a precursor of a repressor inhibiting the synthesis of inducible enzymes. He therefore suggested the term "catabolite repression" as perhaps describing more accurately the glucose effect phenomenon. The catabolite repression hypothesis gives an appealing degree of generality to the glucose effect and explains well the experimental results for β-galactosidase and histidase (*see* 17); however, this hypothesis does not take into account the possibility in some cases for glucose control of enzyme induction by inhibition at the level of inducer transport into the cell. The latter possibility has been suggested by Brown (*see* discussion after reference 16) as a factor in glucose repression of β-galactosidase.

The work reported here suggests that glucose inhibition of induction of the enzymes specific to galactose utilization—the enzymes of the *gal* operon—is exerted mainly at the transport stage, and therefore that, at least in this particular case, the primary mechanism of glucose control is probably not catabolite repression.

MATERIALS AND METHODS

Bacterial strains. The strains of *E. coli* K-12 used, including mutants isolated for the present study, are listed in Table 1.

Genetic techniques. Mutants constitutive for the galactose enzymes were isolated by ultraviolet irradiation and then (i) alternate growth on galactose and glucose for 10 cycles or (ii) plating on galactose plus methyl-β-D-thiogalactoside (TMG) minimal plates. Both techniques have been described by Buttin (1). Recombinant strains and F′/F⁻ diploid strains were isolated by appropriate Hfr × F⁻ and F′ × F⁻ crosses and then plating on selective media. Matings were done as described by Echols (2).

Growth of bacteria and preparation of extracts. Cells were grown at 37 C by rotary shaking in a 2,000-ml Erlenmeyer flask containing 200 ml of 7.0 P medium, which consisted of: KH_2PO_4, 13.6 g; $(NH_4)_2SO_4$, 2 g; $MgSO_4 \cdot 7H_2O$, 0.2 g; $FeSO_4 \cdot 7H_2O$, 0.5 mg; and distilled water, 1 liter; the *p*H was adjusted to 7.0 with KOH prior to sterilization. The carbon sources were added at 0.3% concentration. Amino acids and thiamine, when needed for growth, were supplied at concentrations of 20 and 1 μg/ml, respectively. D-Fucose, when added to induce the galactose enzymes, was used at 10^{-3} *M*.

To prepare extracts for enzyme assays, cells were grown for at least three generations in log-phase growth; cells were then chilled, centrifuged, washed, resuspended, and sonically treated in potassium phosphate-mercaptoacetic acid buffer (23). Sonic treatment was carried out for 3 min in a Raytheon 10-kc oscillator, and the lysate was then centrifuged at 10,000 × *g* for 10 min. The supernatant fluid was stored frozen and was used for kinase, transferase, and epimerase assays within 24 hr. The protein concentration of the extract was determined by use of the Folin reagent (15).

Enzyme assays. Galactokinase (kinase), galactose-1-phosphate uridyl transferase (transferase), and uridinediphosphogalactose-4-epimerase (epimerase) were assayed as reported previously (3).

Inducer uptake measurements. Cells were grown to log phase in 7.0 P medium containing 0.3% glycerol as carbon source, centrifuged, washed with chilled 7.0 P medium, and resuspended in the same medium to give a cell concentration of approximately 4×10^8 per milliliter. The culture was further incubated

TABLE 1. *List of Escherichia coli K-12 strains used*[a]

Strain	Sex	Genotype	Source
FK10W1(A)	F⁻	*lac*⁺ *gal*⁺ *str-r met*⁻	A. Garen
SA2	F⁻	*lac*⁺ *gal*⁺ R^-_{gal} *str-r met*⁻	FK10W1(A), cyclic growth selection for constitutivity
SA3	F⁻	*lac*⁺ *gal*⁺ R^-_{gal} *str-r met*⁻	FK10W1(A), TMG selection for constitutivity
B78A	F⁻	*lac*⁻ (*y*⁻) *gal*⁺ R^-_{gal} *str-r thr*⁻ *leu*⁻ *thi*⁻	G. Buttin (1)
B78A*k*	F⁻	*lac*⁻ (*y*⁻) *gal*⁻ (*k*⁻) R^-_{gal} *str-r thr*⁻ *leu*⁻ *thi*⁻	B78A, kinase⁻
W4580	F′	*gal*⁺ *str-s met*⁻/$F'_{15}R^+_{gal}$ *thy*⁺	Y. Hirota (8)
SA18	F′	*lac*⁺ *gal*⁺ R^-_{gal} *str-r met*⁻/$F'_{15}R^+_{gal}$ *thy*⁺	W4580 × SA3
SA19	F′	*lac*⁺ *gal*⁺ R^-_{gal} *str-r met*⁻/F'_{15} R^+_{gal} *thy*⁺	W4580 × SA2
SA20	F′	*lac*⁻ (*y*⁻) *gal*⁺ R^-_{gal} *str-r thr*⁻ *leu*⁻ *thi*⁻/ F_{15}' $R_{gal}{}^+$ *thy*⁺	W4580 × B78A
H81-2	Hfr	*lac*⁺ *gal*⁺ O^c_{gal} *str-s thi*⁻	G. Buttin (1)
B8	F⁻	*lac*⁻ *gal*⁻ (t_1^- t_4^-) *str-r met*⁻	J. Adler
SA21	F⁻	*lac*⁺ *gal*⁺ O^c_{gal} *str-r met*⁻	H81-2 × B8
3300	Hfr	*lac*⁺ i^-_{lac} *gal*⁺ *str-s thi*⁻	B. Horecker
FK10W1(B)	F⁻	*lac*⁻ *gal*⁺ *str-r met*⁻	A. Garen
SA25	F⁻	*lac*⁺ i^-_{lac} *gal*⁺ *str-r met*⁻	3300 × FK10W1(B)
W3747	F′	*lac*⁺ *gal*⁺ *str-s met*⁻/F'_{13} *lac*⁺ i^+_{lac}	Y. Hirota (5)
SA26	F′	*lac*⁺ i^-_{lac} *gal*⁺ *str-r met*⁻/F'_{13} *lac*⁺ i^+_{lac}	W3747 × SA25

[a] *Met*⁻, *leu*⁻, *thr*⁻, and *thi*⁻ denote the inability to synthesize methionine, leucine, threonine, and thiamine, respectively; *thy*⁺ denotes the ability to synthesize thymine; *lac*⁺ and *gal*⁺, the ability to utilize lactose and galactose, respectively, for growth, and the corresponding negative superscripts, inability to utilize lactose and galactose for growth; *k*⁻, *t*⁻ and *y*⁻, the inability to synthesize galactokinase, galactose-1-phosphate-uridyltransferase, and galactoside permease, respectively; *str-r* and *str-s*, resistance and sensitivity to streptomycin, respectively; R^-_{gal} and O^c_{gal}, constitutive mutations in the regular locus and operator site respectively of the *gal* system; and i^-_{lac}, constitutive mutation in the regulator locus of the *lac* system.

aerobically at 37 C for 20 min to exhaust endogenous metabolites and then was chilled; to 5.0 ml of this culture was added either D-galactose-C^{14}, D-fucose-H^3, or TMG-C^{14} (to give 100 to 1,000 counts per min per mμmole). The concentrations of the radioactive and competing nonradioactive sugars (when added) are specified in the Results section. The culture was incubated at 30 C, and 0.5-ml samples were taken at different times. The samples were filtered through membrane filters (Millipore Filter Corp., Bedford, Mass.), and the filters were then washed three times with 3 ml of ice-cold 7.0 P medium. The filters were dried and counted in a Packard liquid scintillation counter. Zero-time uptake was measured by adding the substrates to cells at 0 C and then filtering. This value was used as background. Units of sugar uptake are millimicromoles of sugar per milliliter of culture having an optical density of 1 at 540 mμ.

Chemicals. Amino acids and nonradioactive TMG were purchased from Mann Research Laboratories, New York, N. Y., and D-galactose-C^{14} and TMG-C^{14} from Volk Radiochemical Co., Burbank, Calif., and New England Nuclear Corp., Boston, Mass., respectively. D-Fucose-H^3 was a gift from J. Adler, and was purified by paper chromatography with *n*-butanol–ethyl alcohol–water (5:1:4) as a solvent system (6). Uridine diphosphogalactose was synthesized in the laboratory of H. G. Khorana according to the method of Roseman et al. (22). Other substrates, cofactors and enzymes used were obtained from Sigma Chemical Co., St. Louis, Mo.

RESULTS

The *gal* operon of *E. coli* contains the linked structural genes for the three enzymes specific to galactose utilization—galactokinase (kinase), galactose-1-phosphate uridyl transferase (transferase), and uridine diphosphogalactose-4-epimerase (epimerase) (1, 10, 14). These three enzymes (which we will call collectively the *gal* enzymes) are coordinately induced by D-galactose (11) and the gratuitous inducer D-fucose (1). Buttin (1) has reported that fucose induction of galactokinase is inhibited by glucose.

Table 2 shows that galactose induction of all three *gal* enzymes, as well as fucose induction, is inhibited by glucose. This is the result expected from the existence of a glucose-galactose diauxie (18). Fructose does not inhibit either galactose or fucose induction, consistent with the absence of a fructose-galactose diauxie in *E. coli* (18).

The inhibition by glucose of induction of the *gal* enzymes could result from either an inhibition of inducer transport or from an intracellular repression of enzyme synthesis. We considered glucose control at the level of transport a strong possibility because previous work by Horecker, Thomas, and Monod (7) and Rogers and Yu (21) demonstrated that glucose can inhibit galactose uptake in *E. coli*, although these investigators did not comment on the possible importance of this in the glucose effect. We have confirmed the glucose inhibition of galactose transport and also demonstrated that glucose inhibits fucose transport.

TABLE 2. *Effect of glucose on inducibility of the gal enzymes: the "glucose effect"*[a]

Carbon source	Enzyme activity		
	Kinase	Transferase	Epimerase
Glycerol	0.9	0.8	1.1
Glycerol + fucose	6.3	8.6	14
Glycerol + galactose	5.9	6.4	8.9
Glucose	0.5	0.9	1.5
Glucose + fucose	0.4	1.0	2.3
Glucose + galactose	0.6	0.8	1.1
Fructose	0.6	1.1	2.3
Fructose + fucose	7.4	8.6	18
Fructose + galactose	8.0	7.9	14

[a] Strain FK10W1(A) was grown overnight in 7.0 P medium with 0.3% glycerol as a carbon source. The overnight culture was diluted 1:100 into 7.0 P containing 0.3% of the carbon sources noted in the table, and cells were grown for at least three generations in log phase to an optical density (540 mμ) of approximately 0.6. Preparation of extracts and enzyme assays were carried out as described in Materials and Methods. Units of enzyme activity are micromoles of product per hour per milligram of protein. Assays of separate extracts from cells of the same strain grown under the same conditions showed approximately the following variability: kinase, ±10%; transferase, ±6% for induced levels of enzyme and ±15% for low enzyme levels; epimerase, ±15% for induced levels of enzyme and ±25% for low enzyme levels.

Figure 1a shows that D-galactose-C^{14} is taken up by an R^- strain (SA3) constitutive for the *gal* enzymes at a high rate; the rate of galactose uptake becomes very low when nonradioactive D-glucose is also present at a 10 times higher concentration. The presence of a 10-fold excess of nonradioactive D-fucose reduced the rate by only 20%. An R^- constitutive strain was used so that galactose permease would be present at a fully induced level (1) without pregrowth on galactose. Figure 1b shows the glucose inhibition in a kinase negative, R^- constitutive strain (B78A*k*) which cannot utilize galactose. We concluded that glucose inhibits galactose transport even if galactose permease is present at a high level, probably because the two sugars share at least a common feature of their transport systems. The results shown in Fig. 1a and 1b suggest that fucose transport may be largely independent of galactose transport. The inability of fucose to inhibit galactose uptake effectively was noted previously by Rogers and Yu (21).

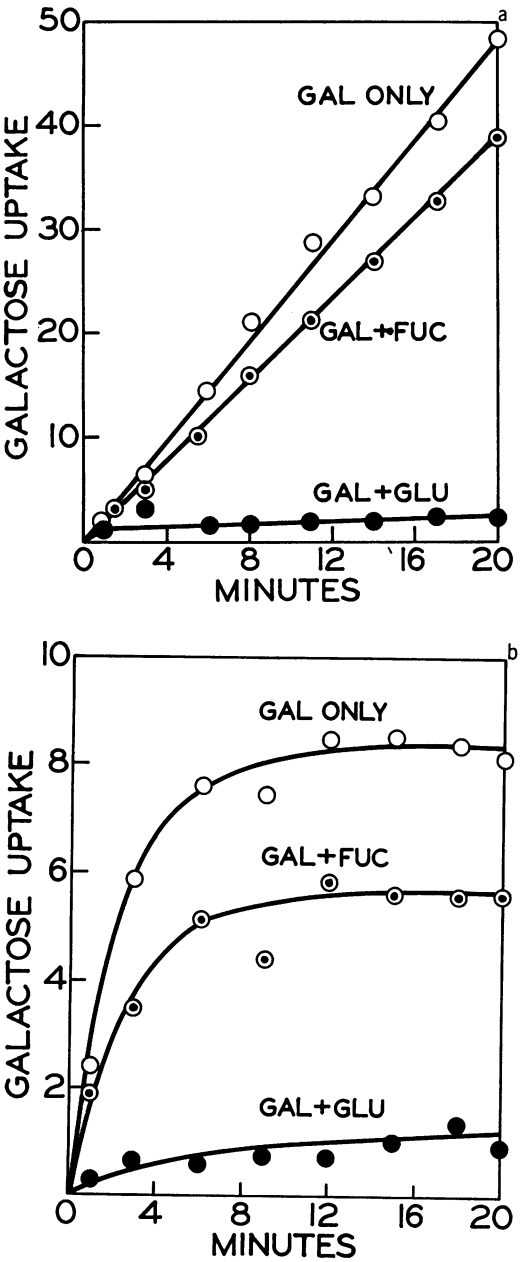

FIG. 1. *Uptake of D-galactose-C^{14} at a concentration of 10^{-3} M by (a) strain SA3, constitutive for the gal enzymes, and (b) strain B78Ak, constitutive and kinase negative: ○, in the absence of a competing sugar; ●, in the presence of 10^{-2} M nonradioactive D-glucose; and ⊙, in the presence of 10^{-2} M nonradioactive D-fucose. Cells were pregrown with 0.3% glycerol as carbon source. The inducer uptake assay was carried out as described in Materials and Methods. Units of sugar uptake are millimicromoles of sugar per milliliter of culture having an optical density of 1 at 540 mμ.*

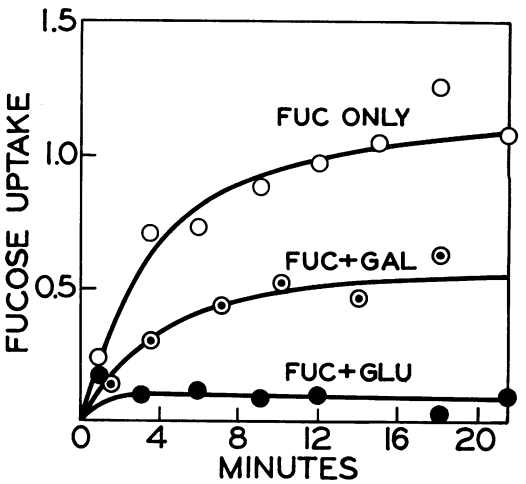

FIG. 2. *Uptake of D-fucose-H^3 at a concentration of 10^{-3} M by strain FK10W1(A), pregrown in glycerol plus galactose: ○, in the absence of a competing sugar; ●, in the presence of 10^{-2} M nonradioactive D-glucose; and ⊙, in the presence of 10^{-2} M nonradioactive D-galactose. Assay procedure and units of sugar uptake are the same as in Fig. 1.*

Uptake of D-fucose-H^3 was found also to be inhibited by glucose (Fig. 2), so that transport of both inducers is glucose-sensitive. Therefore, it seems likely that there are at least two transport systems for glucose, one common to galactose and one to fucose. The fact that fucose uptake is only partially inhibited by a 10-fold excess of galactose supports the interpretation derived from Fig. 1a and 1b, that galactose and fucose transport are largely (but not completely) independent. Ganesan and Rotman (J. Mol. Biol., *in press*) recently obtained evidence that the D-fucose permease is the same as that for methyl-galactoside, but different from the galactose permease (7) and the galactoside permease (20).

The inducer uptake results suggest that inhibition of inducer transport may be the primary mechanism of the glucose effect in the case of glucose inhibition of induction of the *gal* enzymes. Some experiments with a "glucose-resistant" strain strongly support this interpretation. We observed that, in an i^- strain constitutive for the *lac* enzymes (3300), glucose failed to inhibit the galactose induction of transferase but did inhibit fucose induction (Table 3). Since the previous results suggested that glucose inhibits induction of the *gal* enzymes at the transport level, this "escape" of galactose induction might arise from the presence of a separate permease system to take up galactose in this strain. It seemed quite likely that the separate transport system was galacto-

TABLE 3. *Effect of glucose on inducibility of transferase in a galactoside permease constitutive strain*[a]

Carbon sources	Transferase activity
Glycerol	0.7
Glycerol + fucose	5.8
Glycerol + galactose	6.1
Glucose + fucose	0.4
Glucose + galactose	3.9

[a] Strain 3300 (i^-_{lac}) is constitutive for the *lac* enzymes β-galactosidase, galactoside permease, and galactoside acetylase. Cell growth, preparation of extracts, and enzyme assays were carried out as for the assays of Table 2. Units of transferase activity are micromoles of product per hour per milligram of protein.

side permease (20), which is synthesized constitutively in an i^- strain (9).

D-Galactose-C^{14} uptake was observed in strain 3300 (uninduced for the *gal* enzymes) with or without glucose present (Fig. 3). D-Galactose-C^{14} is taken up at a high rate, and the uptake is inhibited only slightly when glucose is present in 10-fold excess. Induction of the *gal* enzymes and galactose transport therefore both show resistance to glucose in strain 3300, a correlation to be expected if glucose normally inhibits at the transport level. That the "escape" of galactose transport in this case is via the galactoside permease usually characterized by TMG uptake (20) is supported by the finding that a 10-fold excess of galactose blocks TMG-C^{14} uptake in strain 3300 (Fig. 4). In contrast, Fig. 4 shows that TMG-C^{14} uptake is not greatly affected by excess glucose.

To confirm that the glucose insensitivity of galactose induction is connected with the i^- character in strain 3300, an i^- *lac*$^+$ F$^-$ strain (SA25) was prepared by a genetic cross and an F′ i^+ *lac*$^+$/ i^- *lac*$^+$ diploid (SA26) constructed from this by F-duction. These strains were assayed for transferase and epimerase after being grown in the absence of an inducer of the *lac* system. From the results (Table 4), it is apparent that galactose induction becomes sensitive to glucose when the cell regains the inducible character for the *lac* enzymes. The classical diauxie phenomenon was also compared in strains SA25 and SA26 (Fig. 5). The i^- strain shows no glucose-galactose diauxie; the i^+/i^- derivative shows the diauxie phenomenon, as expected from the enzyme data.

Studies were also carried out to find out whether there is any evidence for an intracellular repression by glucose. First, enzyme levels were determined in mutant strains which are constitutive for the *gal* enzymes and therefore do not need the

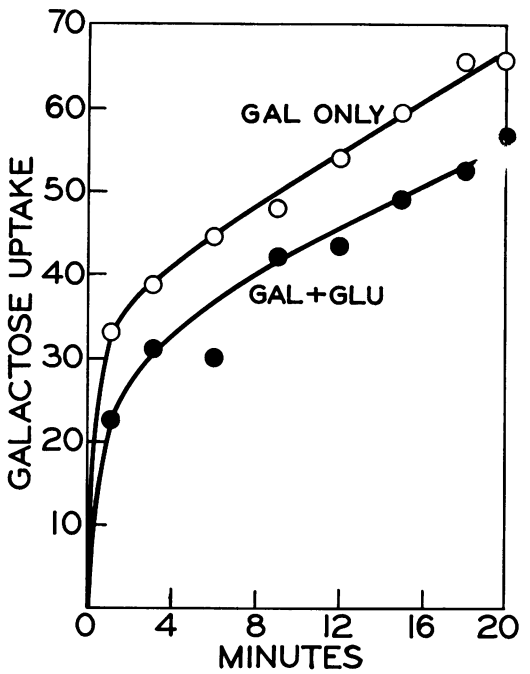

FIG. 3. *Uptake of* D-*galactose-*C^{14} *at a concentration of* 10^{-3} M *by strain 3300 (constitutive for galactoside-permease), pregrown in glycerol:* ○, *in the absence of a competing sugar;* ●, *in the presence of* 10^{-2} M *nonradioactive* D-*glucose. Assay procedure and units of sugar uptake are the same as in Fig. 1.*

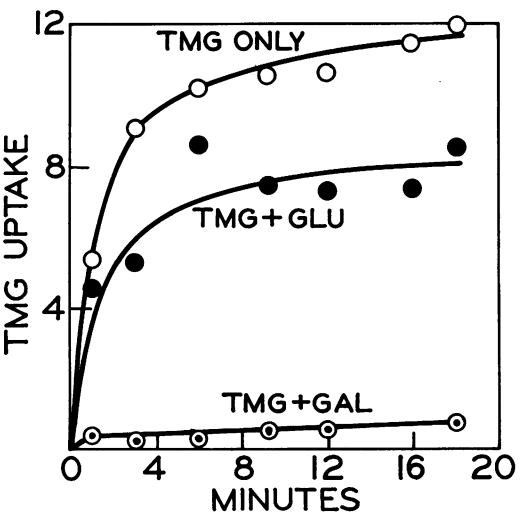

FIG. 4. *Uptake of TMG-*C^{14} *at a concentration of* 10^{-3} M *by strain 3300 (constitutive for galactoside-permease), pregrown in glycerol:* ○, *in the absence of a competing sugar;* ●, *in the presence of* 10^{-2} M *nonradioactive* D-*glucose; and* ⊙, *in the presence of* 10^{-2} M *nonradioactive* D-*galactose. Assay procedure and units of sugar uptake are the same as in Fig. 1.*

TABLE 4. *Effect of carbon source on inducibility of transferase and epimerase in an i^- strain and its F' i^+/i^- derivative*[a]

Strain	Genotype	Galactoside permease	Carbon source	Enzyme activity	
				Transferase	Epimerase
SA25	$F^- i^-$	Constitutive	Glycerol	1.1	0.9
			Galactose	9.4	15
			Galactose + glucose	4.7	12
			Lactose + glucose	3.8	13
SA26	$F' i^+/F^- i^-$	Inducible	Glycerol	1.2	0.8
			Galactose	6.6	21
			Galactose + glucose	0.8	1.3

[a] Growth of strains SA25 and SA26, preparation of extracts, and enzyme assays were carried out as for the assays of Table 2. The i^+ inducible allele is dominant in an i^+/i^- diploid (9). Units of enzyme activity are micromoles of product per hour per milligram of protein.

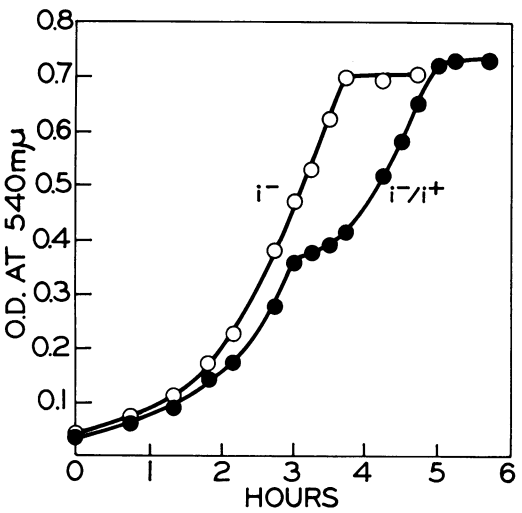

FIG. 5. *Growth curves of strains SA25 (i^-), ○, and SA26 (i^-/i^+), ●, in a mixture of 0.02% galactose and 0.02% glucose. The inocula were grown in glycerol.*

inducer. The effect of glucose on the levels of transferase of some constitutive strains of independent isolation is shown in Table 5. The high enzyme level found on growth in glycerol is diminished only slightly on growth in glucose, irrespective of the genetic origin of the constitutive phenotype [whether from an R^- mutation in the regulator gene or an O^c mutation in the operator site -see genetic analysis of Buttin (1)]. Introduction of an F' *R* factor from an F' R^+/R^+ diploid (W4580) into the F^- R^- constitutive strains brought back both the requirement for the inducer for a high level of enzyme synthesis and strong sensitivity of this induction to glucose (Table 5).

TABLE 5. *Effect of glucose on transferase levels in strains constitutive for the gal enzymes and in inducible F' R^+/R^- derivatives*[a]

Strain	Genotype	Transferase activity			
		Glycerol	Glucose	Glycerol + fucose	Glucose + fucose
SA2	R^-	4.9	3.2	6.8	3.3
SA3	R^-	4.9	3.4	7.9	5.1
B78A	R^-	5.1	4.9	7.0	4.2
SA19	F' R^+/R^-	0.7	0.3	4.8	0.3
SA18	F' R^+/R^-	0.9	0.5	7.0	0.4
SA20	F' R^+/R^-	0.6	0.2	4.2	0.3
SA21	O^c	8.8	5.0	9.2	4.9

[a] Growth of cells, preparation of extracts, and enzyme assays were carried out as for the assays of Table 2. The origin of the strains is given in Table 1. Units of enzyme activities are micromoles of product per hour per milligram of protein.

This is consistent with the idea that glucose is not an effective intracellular repressor. This result, however, could also be explained by a glucose product being a constituent of the *R* gene repressor.

A stronger argument that glucose does not produce pronounced intracellular repression of the *gal* enzymes can be provided by producing the inducer and glucose intracellularly, thus avoiding questions of relative rate of transport of the two compounds. This was done by growing strain SA25 in the presence of 0.3% lactose. Lactose produces galactose and glucose inside the cell by the action of the enzyme β-galactosidase. Additional glucose (0.3%) was also added to the medium to ensure an adequate supply of "glucose repressor." The levels of the *gal* enzymes, trans-

ferase and epimerase, are high under these conditions (line 4 of Table 4), showing that the intracellular mechanism of galactose induction appears to be rather insensitive to glucose inhibition.(Lactose itself was shown not to be an inducer of the *gal* enzymes by its inability to induce the *gal* enzymes in a strain defective in β-galactosidase.)

DISCUSSION

We think that the experiments reported here argue strongly that glucose inhibition of induction of the *gal* enzymes occurs mainly at the level of inducer transport into the cell. We have shown that glucose inhibits uptake of the inducers galactose and fucose and that glucose does not inhibit induction of the *gal* enzymes if glucose and galactose are produced intracellularly by the hydrolysis of lactose. "Glucose-resistant" mutants may be of two types: constitutive for the *gal* enzymes and therefore not requiring an inducer, or constitutive for the *lac* enzymes and therefore acquiring a glucose-resistant alternative transport mechanism for the inducer galactose via galactoside permease. Results and interpretations similar to ours have been independently obtained recently by Stodolsky and Magasanik (*personal communication*).

The inhibition by glucose of galactose uptake was first noted by Horecker, Thomas, and Monod (7), who showed that the inhibition is rather complex in character. Uptake of 10^{-6} M galactose was not inhibited by 10^{-4} M glucose, but uptake of 10^{-4} M galactose was strongly inhibited by 6×10^{-4} M glucose. Horecker et al. (7) suggested that glucose may compete at the level of a common "transporter" substance (12), even though the entrance permeases catalyzing uptake of the external sugars were specific. Competition at a "transporter" level between glucose and TMG under certain conditions was suggested by Kepes (12) and Kessler and Rickenberg (13). In this connection, it is interesting to note that Egan and Morse (4) have isolated single-step mutants of *Staphylococcus aureus* defective in the transport of glucose, galactose, lactose, maltose, sucrose, fructose, and mannitol, and have suggested that these mutant strains are defective in the production of the transporter substance. If similar membrane carriers of such wide specificity exist in *E. coli* and other microorganisms, then many examples of glucose-type effects may represent inhibition of inducer transport at the level of a common transporter substance.

ACKNOWLEDGMENTS

This investigation was supported by Public Health Service grant GM 08407-05 from the Division of General Medical Sciences, and by an institutional grant from the American Cancer Society.

We also appreciate the assistance of Anne Joyner and Opal Larson.

LITERATURE CITED

1. BUTTIN, G. 1963. Mécanismes regulateurs dans la biosynthèse des enzymes du metabolisme du galactose chez *E. coli* K12. J. Mol. Biol. **7**:164–182, 183–205.
2. ECHOLS, H. 1963. Properties of F′ strains of *Escherichia coli* superinfected with F-lactose and F-galactose episomes. J. Bacteriol. **85**:262–268.
3. ECHOLS, H., J. REZNICHEK, AND S. ADHYA. 1963. Complementation, recombination and suppression in galactose negative mutants of *E. coli*. Proc. Natl. Acad. Sci. U.S. **50**:286–293.
4. EGAN, J. B., AND M. L. MORSE. 1965. Carbohydrate transport in *S. aureus*. I. Genetic and biochemical analysis of a pleiotropic transport mutant. Biochim. Biophys. Acta **97**:310–319.
5. HIROTA, Y. 1959. Mutants of the F-factor in *E. coli* K-12. Records Genet. Soc. Am. **28**:75.
6. HIRST, E. L., AND J. K. N. JONES. 1949. The application of partition chromatography to the partition of sugars and their derivatives. Discussions Faraday Soc. **7**:268–274.
7. HORECKER, B. L., J. THOMAS, AND J. MONOD. 1960. Galactose transport in *E. coli*. J. Biol. Chem. **235**:1580–1585, 1586–1590.
8. ISHIBASHI, M., Y. SUGINO, AND Y. HIROTA. 1964. Chromosomal location of thymine and arginine genes in *Escherichia coli* and F′ incorporating them. J. Bacteriol. **87**:554–561.
9. JACOB, F., AND J. MONOD. 1961. Genetic regulatory mechanisms in the synthesis of proteins. J. Mol. Biol. **3**:318–356.
10. JORDAN, E., M. B. YARMALINSKY, AND H. KALCKAR. 1962. Control of inducibility of enzymes of the galactose sequence in *E. coli*. Proc. Natl. Acad. Sci. U.S. **48**:32–40.
11. KALCKAR, H., K. KURAHASHI, AND E. JORDAN. 1959. Hereditary defects in galactose metabolism in *E. coli* mutants. I. Determination of enzyme activities. Proc. Natl. Acad. Sci. U.S. **45**:1776–1791.
12. KEPES, A. 1960. Études cinétiques sur la galactoside-permease d'*E. coli*. Biochim. Biophys. Acta **40**:70–84.
13. KESSLER, D. P., AND H. V. RICKENBERG. 1963. The competitive inhibition of α-methylglucoside uptake in *E. coli*. Biochem. Biophys. Res. Commun. **10**:482–487.
14. LEDERBERG, E. L. 1960. Genetic and functional aspects of galactole metabolism in *E. coli* K-12, p. 115. *In* W. Hayes and R. C. Clowes [ed.], Microbial genetics. Cambridge Univ. Press, London.
15. LOWRY, O. H., N. J. ROSEBROUGH, A. L. FARR, AND R. J. RANDALL. 1951. Protein measurement with the Folin phenol reagent. J. Biol. Chem. **193**:265–275.
16. MAGASANIK, B. 1961. Catabolite-repression. Cold Spring Harbor Symp. Quant. Biol. **26**:249–256.

17. MAGASANIK, B. 1963. The genetic and molecular basis of catabolite repression, p. 271. *In* H. Vogel, V. Bryson, and J. Lampen, Informational macromolecules. Academic Press, Inc. New York.
18. MONOD, J. 1942. Recherches sur la croissance des cultures bacteriennes. Hermann et Cie, Paris.
19. MONOD, J. 1947. The phenomenon of enzymatic adaptation. Growth **11**:223–289.
20. RICKENBERG, H. V., G. N. COHEN, G. BUTTIN, AND J. MONOD. 1956. La galactoside-permease d'*Escherichia coli*. Ann. Inst. Pasteur **91**:829–857.
21. ROGERS, D., AND S.-H. YU. 1962. Substrate specificity of a glucose permease of *Escherichia coli*. J. Bacteriol. **84**:877–881.
22. ROSEMAN, S., J. DISTLER, J. MOFFATT, AND H. G. KHORANA. 1961. Nucleoside polyphosphates. XI. An improved general method for the synthesis of nucleotide co-enzymes. J. Am. Chem. Soc. **83**:659–663.
23. SHERMAN, J., AND J. ADLER. 1963. Galactokinase from *E. coli*. J. Biol. Chem. **238**:873–878.