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In Vitro and In Vivo Effects of Soluble, Monovalent Globotriose on Bacterial Attachment and Colonization

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Epithelial cells lining the urinary tract are rich in globo series glycolipids, structurally defined by a Galα1,4Gal motif in the oligosaccharide moiety of this glycolipid family. This Galα1,4Gal motif is the attachment target for the P-fimbrial adhesin of uropathogenic *Escherichia coli*. We investigated the ability of a trisaccharide analog of this core motif, globotriose (Galα1,4Galβ1,4Glc), to interfere with uropathogen attachment and colonization in vitro and in vivo. We assessed the ability of globotriose to inhibit and reverse the binding and agglutination of a P-fimbriated strain of *E. coli* (JR1) using human erythrocytes and immortalized human colonic epithelial cells as targets. Globotriose (5 mg/ml) completely inhibited and reversed cell agglutination and caused a 10- to 100-fold reduction in JR1 binding to target cells, as determined by flow cytometry. In preparation for an in vivo efficacy study, we investigated the distribution and pharmacokinetics of globotriose in the BALB/c mouse. Globotriose was administered via the tail vein, targeting an instantaneous plasma concentration of 5 mg/ml, and in a different experiment, animals were gavaged at 10 times the intravenous (i.v.) dose. Globotriose was rapidly cleared from plasma (half-life [$t_{1/2}$], 6 min) and slowly excreted via the kidney ($t_{1/2}$, 4 h). Urine levels of >5 mg/ml were maintained from 4 to 12 h after the i.v. bolus dose, which resulted in a 1-log reduction in established bladder colonization by JR1. These results suggest that free, soluble globotriose is a feasible alternative therapy for urinary tract infections.

Glycolipids and other cell surface glycoconjugates play important roles in tissue development, cell trafficking and sorting, and cell-cell recognition. Independently of their inherent biological functions, cell surface glycolipids are used as targets by bacteria, viruses, and toxins to recognize and adhere to cells. Several groups have described and proposed the use of oligosaccharides to prevent or reverse pathological events occurring at the cell surface (7, 14, 15). This oligosaccharide receptor decoy concept is based on a rich body of experimental evidence demonstrating the importance of cell surface oligosaccharides in health and disease. Microbial lectins have been shown to have low affinities for their monovalent carbohydrate binding targets (4, 5), and carbohydrate targets of microbial lectins are normally present in a multivalent fashion on mammalian cell surfaces. The microbial lectins themselves are often displayed as multivalent complexes, or, as is the case with many microbial toxins, each contains a multimeric carbohydrate binding subunit. This multivalent presentation of binding targets and microbial lectins drives the equilibrium strongly in favor of the formation of target-ligand pairs. For these reasons, multivalent glycoconjugates have been favored for development as antiadhesive therapeutic candidates, despite the difficulties associated with the synthesis and the poor bioavailability of multivalent preparations.

Recently, reports describing methods for the large-scale synthesis of high-purity monovalent oligosaccharides and other glycoconjugates have surfaced (6, 9, 10). The synthesis technologies described in these reports have resulted in the availability of oligosaccharides previously obtained only in minute quantities by either chemical or enzymatic release from glycolipids; additionally, these novel technologies reduce synthesis costs, thus making oligosaccharide-based therapies legitimate targets for development. Despite the low affinities of microbial lectins for monovalent oligosaccharides containing their target epitopes, these structures are plausible drug candidates, given their wide distribution on exposed cell surfaces and their apparent metabolic stability, assuming that they can be delivered to relevant tissues and at appropriate concentrations.

The cell surface glycolipids of the globo series are defined by the presence of neutral extracellular carbohydrate moieties containing the Galα1,4Gal motif. This unique structure has been shown to be the target for a variety of microbial lectins in humans and animals. One of these is the P-fimbrial adhesin of uropathogenic *Escherichia coli*. *E. coli* causes 75 to 80% of all urinary tract infections (UTIs) (1, 18) and is considered the model uropathogen. Disease-causing strains of *E. coli* express a number of well-studied virulence factors, with the P-fimbrial adhesin being the one that correlates the most with uropathogenicity (12). While it is found on only 5 to 10% of human fecal *E. coli* isolates, the P-fimbiral adhesin is present on 50 to 65% of strains that cause cystitis and 75 to 90% of the strains that cause pyleonephritis (13). Three glycolipids of the globo series are highly expressed on the epithelial cells that line the human urinary tract and kidney (16) and are recognized and bound with a high affinity by the P-fimbrial adhesin. The Galα1,4Gal disaccharide is the minimum P-fimbrial binding epitope (3). The trisaccharide globotriose (Galα1,4Galβ1,4Glc) is a low-molecular-weight analog of this core globo series glycolipid carbohydrate. Several groups have demonstrated that glycolip-

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ids and oligosaccharides which contain Galα1,4Gal epitopes can effectively inhibit the attachment of UTI-causing *E. coli* strains bearing the P-fimbrial adhesin to target cells (16, 17, 11). We have extended these observations by demonstrating that the free, soluble trisaccharide globotriose can prevent and reverse the binding of P-fimbriated *E. coli* in vitro and can be administered orally or intravenously (i.v.) with no acute toxicity.

MATERIALS AND METHODS

Bacteria and cells. *E. coli* JR1 (American Type Culture Collection [ATCC]), a clinical isolate uropathogenic for humans, was grown in Trypticase soy broth at 37°C; and cultures were passaged every 48 to 72 h. To express the P fimbria for in vitro studies, the bacteria were grown on colonization factor antigen agar plates overnight. Two target cells that express globoside were used for in vitro experiments: type A1 Rh-positive P1-positive red blood cells (RBCs; the American Red Cross) and cells of the HT29 human colonic adenocarcinoma cell line (ATCC).

Animals. Female BALB/c mice ($n = 125$; age, 8 to 10 weeks; weight, ~30 g) were purchased from Charles River, Inc. The mice were housed in groups (a maximum of five mice per metabolism cage) in an environmentally controlled room (25 ± 2°C with a 12-h light, 12-h dark cycle) in accordance with the guidelines of the Institutional Animal Care Use Committee and the American Association for the Accreditation of Laboratory Animal Care standards.

Slide agglutination assay. To study the inhibition of binding of P-fimbriated *E. coli* to target cells, 10 μl of either RBCs at 1×10^8 cells/ml or HT29 at 1×10^7 cells/ml was combined with JR1 bacteria at 1×10^9 bacterial cells/ml and with 10 μl of saccharide solution (final concentration, 5 mg/ml). The mixtures were incubated for 2 min under motion and were observed under a light microscope. To determine the reversal of binding, the bacteria and target cells were allowed to agglutinate for 15 min, and oligosaccharide solutions were added afterwards. The mixtures were incubated under motion for 15 min.

Flow cytometry assay. FLUOS-labeled bacteria (labeling was performed according to the instructions of the manufacturer [Boehringer Mannheim]) were diluted to 1×10^8 bacterial cells/ml, the human AP1 RBCs were diluted to 1×10^7 cells/ml, and HT29 cells were diluted to 5×10^6 cells/ml. To test the ability of globotriose to prevent the binding of the bacteria to the target cells, 50 μl of bacteria suspension, 50 μl of target cells, and 900 μl of phosphate-buffered saline (PBS) or saccharide solution (globotriose, galactotriose, mannose, or lactose) were diluted to 5 to 20 mg/ml in PBS. The mixtures were incubated under motion at 37°C for 30 min, vortexed, and analyzed on the flow cytometer. To test the ability of globotriose to reverse the binding of the bacteria to the target cells, the same protocol was used, except that the bacteria and the cells were allowed to incubate together for 30 min while the mixture was rocked at 37°C before the PBS or saccharide solution was added. For both types of assays, a stop point of 120 s or 10,000 target cells was used.

Plate-based button agglutination assay. A button agglutination assay was used to estimate the minimum effective antiadhesive dose of globotriose. Ten microliters of human type AP1 RBCs at 1×10^8 cells/ml was combined with 10 μl of JR1 bacteria at 1×10^9 bacterial cells/ml and with 10 μl of saccharide solution in duplicate wells of a standard 96-well plate. Agglutination was scored visually by the size of the button formed by the target cell-bacteria mixture in the wells. One set of duplicate wells contained only AP1 RBCs as a negative control and were assigned a score of 0 for no agglutination (small, dense button). One set of duplicate wells contained only AP1 cells and JR1 as a positive control and were assigned a score of 3 for complete agglutination (large, diffuse button). Sets of duplicate wells for the following saccharide-negative controls were included: 20 mg/ml lactose, 20 mg/ml glucose, 10 mg galactotriose (Galβ1,4Galβ1,4Gal), 20 mg/ml fucose, and 20 mg/ml mannose. Duplicate wells containing AP1 RBCs, JR1, and globotriose at 10 mg/ml and at six twofold dilutions thereof were prepared to estimate the minimum effective globotriose concentration. The experiment was carried out at room temperature, and agglutination was scored after 5 min incubation.

Pharmacokinetic study. (i) i.v. phase. To determine plasma pharmacokinetics and the kinetics of elimination, 45 female BALB/c mice were dosed with 286.14 mg globotriose per kg body weight via the tail vein by i.v. injection (average dose volume, 120 μl of a 42.8-mg/ml globotriose solution). Terminal blood samples were colleted via cardiac puncture from 13 groups of three mice each at time points ranging from 2 min to 16 h postdosing. Urine and feces were collected from a separate group of five mice for 24 h (in 4-h increments) postdosing, and the same mice were used to collect a 24-h postdosing blood sample via cardiac puncture. Plasma was collected from all blood samples. Plasma, urine, and feces were analyzed for globotriose by high-pressure liquid chromatography (HPLC). Plasma and urine were diluted with an equal volume of 10% acetonitrile–water (vol/vol) to achieve a final acetonitrile concentration of 5% (vol/vol). Fecal samples were placed in a closable glass vial and diluted with water to a weight 10 times that of the fecal sample. Two or three 4-mm glass beads were added to the samples, and the sample vials were capped and heated in a boiling water bath with occasional vortexing for 10 to 20 min. The samples were cooled to room temperature and vortexed vigorously, and an aliquot of the homogeneous mixture was rapidly transferred to a 0.5-ml plastic centrifuge tube. The samples were vortexed at 3,000 relative centrifugal force for 20 min at 5°C. A known volume of the clear, particulate-free upper layer was transferred to an HPLC sample vial and diluted with 10% acetonitrile-water (vol/vol) to a final acetonitrile concentration of 5% (vol/vol). Globotriose was measured by high-pH anion-exchange chromatography with pulsed amperometric detection by using two Dionex CarboPac PA100 analytical columns, one Dionex CarboPac PA100 guard column, and a sodium hydroxide-sodium acetate mobile phase gradient composition.

(ii) Oral phase. To assess the bioavailability of orally ingested globotriose, 40 BALB/c mice were dosed with 2,842.24 mg globotriose per kg of body weight via oral gavage (average dose volume, 300 μl of a 51.15-mg/ml globotriose solution). Terminal blood samples were colleted via cardiac puncture from 12 groups of three mice each at time points ranging from 5 min to 24 h postdosing. Urine and feces were collected from a separate group of five mice for 48 h (in 4-h increments through 16 h, one 8-h increment from 16 to 24 h, and one 24-h increment to 48 h) postdosing, and the same mice were used to collect a 48-h postdosing blood sample via cardiac puncture. Plasma was collected from all blood samples. Plasma, feces, and urine were also tested by HPLC, as described above.

Efficacy study: UTI treatment. To test the efficacy of globotriose in vivo, a proof-of-principle study was performed by using a BALB/c mouse model of human UTI (2). Two studies were conducted: a test of the ability of globotriose to prevent colonization of the mouse bladder by JR1 and a test of the ability of globotriose to reverse established bladder colonization. Each protocol consisted of a group treated with globotriose ($n = 10$) and a placebo group administered the saline vehicle ($n = 10$). Based on the results of in vitro studies, the efficacious concentration of globotriose was determined to be about 5 mg/ml globotriose in the urine. The results of the pharmacokinetic study demonstrated that this level of globotriose could be maintained in the urine from about 4 to 16 h after i.v. administration of globotriose at a dose of 333 mg/kg. All treated mice were dosed with globotriose at this level by intravenous injection in the tail vein, and the placebo group of mice was dosed with saline by intravenous injection in the tail vein. In both experiments, anesthetized mice were intraurethrally inoculated with a minimum of 10^8 JR1 *E. coli* bacteria in 25 μl sterile saline. For the prevention protocol mice were dosed with globotriose or vehicle 4 h prior to inoculation with JR1 and again 8 h after inoculation. For the treatment protocol, mice were dosed with globotriose or vehicle 24 and 36 h after inoculation. Urine was collected from each group before dosing and approximately 12 h after the administration of each dose. The mice were killed 48 h after administration of the initial i.v. dose, and their bladders were aseptically removed. The bladders were homogenized, and 1:50 dilutions of the resulting homogenates were streaked on three Levine's eosin-methylene blue agar plates. After overnight incubation at 37°C, the numbers of CFU were counted, and the ratio CFU/mg bladder was calculated as an index of antiadherence. Urine was also analyzed for the relative number of *E. coli* cells by flow cytometry and HPLC.

RESULTS

Effects of globotriose on agglutination and binding of JR1 to target cells. A standard agglutination assay was used to test the ability of globotriose to prevent and reverse P fimbria-mediated agglutination of *E. coli* JR1 with human AP1 red blood cells and HT29 cells as targets. Agglutination was completely inhibited when 5 mg/ml globotriose was added simultaneously with the bacteria and the target cells. Similarly, agglutination was rapidly and completely reversed when 5 mg/ml globotriose was added to the bacteria and target cells after agglutination had already occurred (Fig. 1). Glucose, mannose, lactose (Galβ1,4Glc), and the trisaccharide galactotriose (Galβ1, 4Galβ1,4Gal) had no effect on agglutination when they were added before or after the formation of multicellular com-

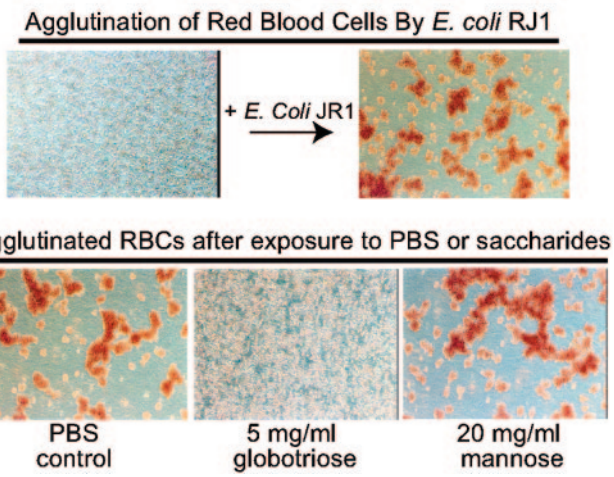

FIG. 1. Slide agglutination assay of AP1 red blood cells and monovalent, free oligosaccharides. The top two panels show the agglutination of human red blood cells that express the P antigen (contained in the glycolipid globoside) in the presence of uropathogenic *E. coli*, as described in Materials and Methods. The lower panels show that the agglutination of red blood cells and uropathogenic *E. coli* JR1 could be prevented or reversed only by globotriose.

plexes. The ability of globotriose to prevent the binding of *E. coli* JR1 to human AP1 red blood cells was assessed by flow cytometry. Subagglutinating numbers of fluorescein-labeled JR1 were mixed with target cells in the presence of globotriose or control saccharides, and the target cell-associated green fluorescence was measured. Globotriose at 5 mg/ml caused a 10-fold reduction in the mean target cell fluorescence, whereas galactotriose, mannose, and lactose had no effect on target cell fluorescence (Fig. 2). A 96-well plate-based assay was used to

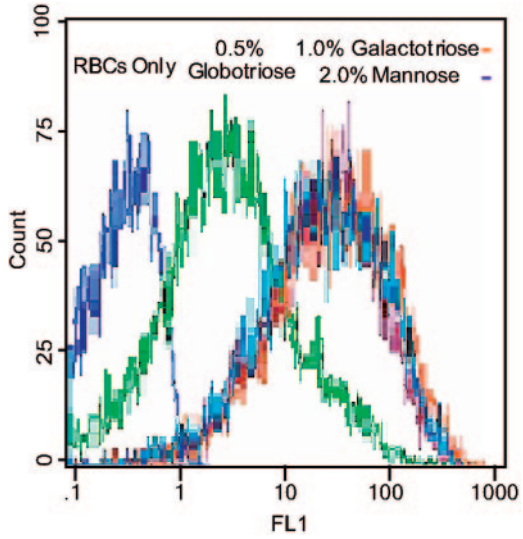

FIG. 2. Binding of fluorescein-labeled JR1 to human AP1 red blood cells, as monitored by flow cytometry. Fluorescein-labeled JR1 cells were incubated with human AP1 red blood cells in the presence of various oligosaccharides, and the red blood cell-associated green fluorescence was monitored. Globotriose at 5 mg/ml reduced the red blood cell-associated green fluorescence 10-fold, while control oligosaccharides (5 mg/ml galactriose, 20 mg/ml mannose) had no effect.

TABLE 1. Specificity and dose-response of inhibition of agglutination by globotriose

Condition	Score[a]
AP1 red blood cells only (defined as no agglutination)	0
AP1 and JR1 (defined as complete agglutination)	3
AP1 target cells and JR1 plus 20 mg/ml mannose, 10 mg/ml galactoriose (Galβ1, 4Galβ1, 4Gal), 20 mg/ml lactose, 20 mg/ml glucose, or 20 mg/ml fucose	3
AP1 target cells, JR1, plus globotriose at 10, 5, 2.5, or 1.25 mg/ml (18.5 to 2.3 mM)	1
AP1 target cells and JR1, plus globotriose at 0.613 mg/ml (1.1 mM)	2
AP1 target cells, JR1, plus globotriose at 0.306 or 0.153 mg/ml (0.57, 0.28 mM)	3

[a] 1, minimal agglutination; 2, moderate agglutination; 3, complete agglutination.

determine the minimum level of globotriose effective for the inhibition of P-fimbria-mediated agglutination. In this assay, globotriose at 10, 5, 2.5, and 1.25 mg/ml completely inhibited agglutination. Partial inhibition was achieved with 0.625 mg/ml globotriose, and no effect on agglutination was seen at 0.312 and 0.156 mg/ml, as shown in Table 1.

Pharmacokinetic study. A study performed to understand the pharmacokinetics, distribution, and excretion of globotriose was conducted in the BALB/c mouse, in preparation for an in vivo efficacy study. Prospectively, the goal was to administer a single dose of globotriose such that a level of 5 mg/ml in urine was attained and maintained for a substantial period of time. To this end, globotriose was administered intravenously via the tail vein at a dose intended to produce an instantaneous level of 5 mg/ml in the blood compartment (target, 333 mg/kg) and orally via gavage at a dose 10 times the i.v. dose. The key pharmacokinetic parameters are presented in Table 2, while plots of the plasma and urine levels of globotriose versus time resulting from the intravenous dosing are shown in Fig. 3. Urinary excretion data are presented in Table 3. In the intravenous portion of the study, the instantaneous plasma concentration was about half the target dose (zero time intercept for the α phase $[A] = 2.3$ mg/ml) and the trisaccharide was rapidly cleared from the plasma compartment (distribution-phase half-life $[t_{1/2\alpha}]$ 5.91 min) and was distributed into the body spaces of the animal. Globotriose was slowly and primarily excreted in the urine (Tables 2 and 3), although it was not detected in urine collected up to 4 h postdosing. Conversely, urine collected from 4 to 8 h and 8 to 12 h contained concentrations well above the prospective efficacious target level of 5 mg/ml. At the conclusion of the 24-h i.v. administration phase

TABLE 2. Pharmacokinetics of globotriose following administration of single bolus intravenous and oral doses to mice

Parameter	Intravenous	Oral
Dose (mg/kg)	286.14	2,842.24
AUC_∞[a] (μg · min/ml)	30,144.63	6,715.83
Oral bioavailability		0.022
Peak serum concn (μg/ml)	2,298.65 (A)	21.20 (C_{max})
$t_{1/2\alpha}$ (min)	5.91	
$t_{1/2\beta}$ (min)		235.29
Cumulative % excretion from 0 to 24 h		
Urine	65%	
Feces	3%	

[a] AUC_∞, area under the concentration-time curve at infinity.

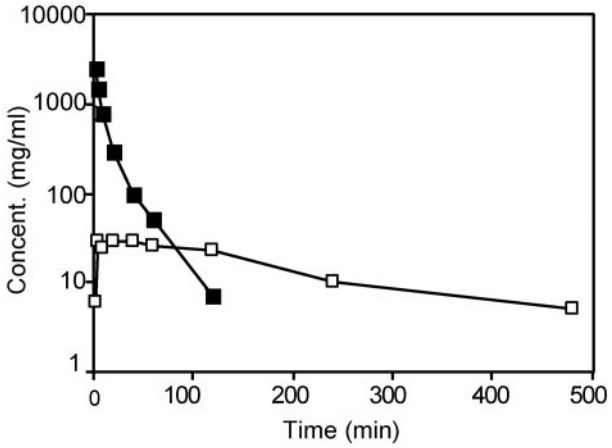

FIG. 3. Serum concentrations following dosing of globotriose in mice. Globotriose was administered to mice intravenously and orally, as described in the text. Serum concentrations (Concent.) of the oligosaccharide were monitored: ■, intravenous dose values; □, oral dose values. The pharmacokinetic study indicated rapid clearance from the serum compartment into the total body water and slow excretion, primarily via urine.

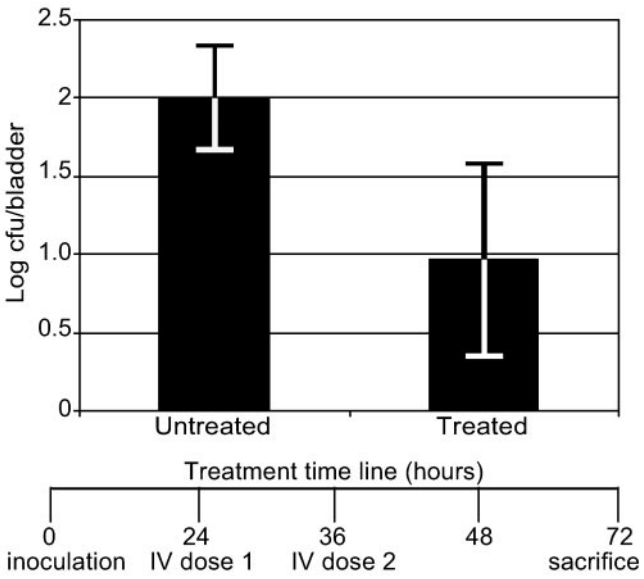

FIG. 4. Comparison of *E. coli* JR1 experimental infection in mice treated or not treated with globotriose. Mice that were intraurethrally inoculated with *E. coli* were given two i.v. doses of 333 mg/kg of globotriose, as indicated on the time line at the bottom of the figure. The bladders were excised after the mice were killed and were assayed for the numbers of CFU. Bladders from mice treated with globotriose showed a 1-log reduction in infection ($P = 0.0153$).

of the study, >65% of the dose had been excreted into the urine and 3% of the dose was excreted in feces. There were insufficient data from the plasma levels after i.v. administration to calculate an elimination-phase half-life ($t_{1/2\beta}$). However, both the plasma levels after oral administration and urinary excretion after i.v. administration support an elimination half-life of 4 to 6 h. There were no indications of adverse effects with the intravenously administered globotriose. Orally administered globotriose was rapidly absorbed from the gastrointestinal tract, with a maximum concentration in plasma of (C_{max}) of 21.20 μg/ml and a time to C_{max} of 15 min and. This rapid approach to C_{max} suggests that absorption is not rate limiting and that the phase after C_{max} is representative of the actual elimination phase. Based on the plasma levels after oral administration, the terminal elimination-phase half-life was 235.29 min and the oral bioavailability was 2.2%. Most of the orally administered globotriose passed through the animal without metabolism and was excreted in the feces. The oral dose was high, and the feces collected from 8 to 12 h and 12 to 16 h postdosing were more than 10% by weight globotriose. This high level of unabsorbed oligosaccharide apparently acted as an osmotic laxative, causing 25 of the orally dosed animals to have soft stools and 5 of these to have frank diarrhea. Because of the construction of the metabolism cages housing the animals and the soft stools, the urine samples from the oral dosing phase of the study appear to have been significantly contaminated with globotriose from the feces. One key observation from urine and fecal excretion in both the i.v. and the oral dosing arms of the study is that globotriose is excreted significantly and possibly completely without metabolic modification.

TABLE 3. Urinary excretion of globotriose after i.v. administration

Time interval (h)	Concn (mg/ml)	Cumulative % dose excreted
0–4	<0.025	0
4–8	16.5	6.9
8–12	12.9	39.1
12–16	1.10	43.9
16–24	2.50	65.8

In vivo UTI study. The efficacy of globotriose as an inhibitor of uropathogenic colonization was tested in vivo by using a BALB/c mouse model of human UTI. All treated animals were intravenously dosed (tail vein) at 333 mg/kg, a level shown to maintain urine globotriose levels above 5 mg/ml for 4 to 12 h after administration. The levels of colonization of the bladders of the treated and the untreated animals from both the prevention and treatment arms of the study were lower than those in previously published studies (2). Colonization rates in the prevention arm of the study were especially low and erratic, and there were no differences in the mean log CFU/bladder values between the control and the globotriose groups. In the treatment arm of the study, mice administered globotriose showed a statistically significant ($P = 0.0153$) 1-log reduction in colonization with bacteria compared to that of the saline-dosed controls (Fig. 4).

DISCUSSION

The present account describes the use of a free oligosaccharide to inhibit and reverse specific bacterial attachment to target cells by using in vitro techniques, which led to in vivo experimentation with animal models. The in vitro data presented here demonstrate that a monovalent analog of the carbohydrate binding motif for the P-fimbrial microbial lectin can prevent and reverse its binding. Published dissociation con-

stants of microbial lectins for their carbohydrate ligands are in the high micromolar to low millimolar range (4, 5). The results presented here show that globotriose completely inhibits agglutination down to a concentration of 1.25 mg/ml (2.3 mM), is partially effective at 0.625 mg/ml (1.15 mM), and is ineffective below 0.3125 mg/ml (580 μM); all of these values are in agreement with those published previously. A concentration of 5 mg/ml was chosen as the efficacious antiadhesive level because it is about 10-fold higher than the published dissociation constants and the experimental observations and because it consistently and robustly inhibited agglutination and binding. The pharmacokinetic behavior of the oligosaccharide was studied to determine the feasibility of conducting preliminary animal trials for detection of its biological activity. This pharmacokinetic study suggests that globotriose is well tolerated when it is delivered intravenously, even at high dosages. It is interesting that globotriose is rapidly distributed into the body water rather than remaining in circulation. This unexpected phenomenon may be helpful because it allows the oligosaccharide to be slowly released back into the bloodstream over a longer period of time (>24 h) and then excreted by the kidneys without metabolism. The oral pharmacokinetics of globotriose also show promise. At the high dose administered in this study, globotriose has a modest bioavailability, as assessed by determination of levels in plasma. Our study suggests, however, that orally delivered globotriose is also rapidly distributed into the total body water of the animal and is slowly rereleased into the bloodstream, thus providing a useful half-life. Future studies should include pharmacokinetic assessment with repeated oral administration below a level that will act as an osmotic laxative to determine if the whole animal (as opposed to the plasma compartment) can be loaded with a globotriose level that will result in the delivery of efficacious levels to the urine. Another promising result is the lack of apparent gastrointestinal metabolism and the ability to deliver large amounts of this oligosaccharide to the colon. This characteristic may work well in receptor decoy applications for pathogenic gastrointestinal bacterial colonization.

The reduced colonization of mouse bladders following intravenous dosing of globotriose extends the findings of previous studies. Other investigators (8, 17) demonstrated that small-molecule sugars can be used to inhibit the colonization of target organs in an artificial manner. For instance, Svanborg-Eden and coworkers (17) preincubated uropathogenic *E. coli* with a receptor analogue carbohydrate and then inoculated the mouse with the mixture to demonstrate that the ability of the bacteria to bind to the bladder epithelium had been inhibited by the receptor analogue. The results described in this report demonstrate that a receptor analogue can be delivered unmolested and at concentrations efficacious against the target organ via the bloodstream. In addition, globotriose can inhibit the binding of uropathogens to the bladder epithelium in the complex matrix of urine. Globotriose can also reverse the binding of the pathogen to the bladder epithelium once it has attached. Finally, our results show that competitive inhibition can be achieved with a monovalent oligosaccharide. This initial study proves that receptor analogue sugars may have efficacy as alternative treatments for urinary tract infections. Further studies are needed to test the efficacy of this molecule for the prevention of infections caused by uropathogenic bacteria and for the treatment of established infections.

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