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# Fimbria-Mediated Adherence of *Candida albicans* to Glycosphingolipid Receptors on Human Buccal Epithelial Cells

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***Candida albicans* is an opportunist fungal pathogen that has the ability to adhere to host cell surface receptors via a number of adhesins. Yu et al. (L. Yu, K. K. Lee, K. Ens, P. C. Doig, M. R. Carpenter, W. Staddon, R. S. Hodges, W. Paranchych, and R. T. Irvin, Infect. Immun. 62:2834–2842, 1994) described the purification and initial characterization of a fimbrial adhesin from *C. albicans*. In this paper, we show that *C. albicans* fimbriae also bind to asialo-$GM_1$ [gangliotetraosylceramide: βGal(1-3)βGalNAc(1-4) βGal(1-4)βGlc(1-1)Cer] immobilized on microtiter plates in a saturable and concentration-dependent manner. *C. albicans* fimbrial binding to exfoliated human buccal epithelial cells (BECs) was inhibited by asialo-$GM_1$ in in vitro binding assays. The fimbriae interact with the glycosphingolipid receptors via the carbohydrate portion of the receptors, since fimbriae were observed to bind to synthetic βGalNAc(1-4)βGal–protein conjugates and the disaccharide was able to inhibit binding of fimbriae to BECs in in vitro binding assays. We conclude from these results that the *C. albicans* yeast form expresses a fimbrial adhesin that binds to glycosphingolipids displayed on the surface of human BECs.**

The adherence of *Candida albicans* to host cells is believed to play a critical role in colonization of mucosal surfaces and subsequent infection (14, 37). *C. albicans* has been demonstrated to bind to buccal epithelial cells (BECs) (33, 35, 44, 64), vaginal epithelial cells (42, 63), human corneocyte cells (7, 53), vascular endothelial cells (38, 47, 56), fibrin-platelet matrix (45), and plastic surfaces (55, 56, 58). Adherence of *C. albicans* to mucosal epithelial cell surfaces is influenced by a number of factors, including temperature (42), pH (51), antibiotic treatment (29), phenotypic state (30), growth media (48), commensal bacteria (6, 32, 46), germ tube formation (34), and tissue sites (59). More extensive reviews of the factors affecting *C. albicans* adherence to epithelial cells in vivo and in vitro are available (11, 12, 29). *C. albicans* adherence to human BECs is somewhat strain dependent (28). A number of potential *C. albicans* adhesins have been identified and include the extracellular polymeric material (8, 13, 49, 65), acid proteinase (2, 18, 54), and chitin (60). In addition, *C. albicans* may express hydrophobic molecules that could mediate attachment to cell surfaces through hydrophobic interactions (21–24). A common feature of these proposed adhesins is that they all appear to be mannoproteins (9). Additionally, a role for *Candida* lipids in adherence has also been proposed by Ghannoum et al. (19).

The expression of *Candida* adhesins appears to be influenced by the phenotypic and dimorphic states of the organism (3, 14, 23, 30, 31, 34). Environmental factors may also regulate the expression of *C. albicans* adhesins (49). It is very likely that multiple adhesins are employed by *C. albicans* in adhering to cell surfaces (39, 64) and that different host cell membrane receptors are involved in these interactions (4, 9). It is not known just how many classes of host cell receptors are involved in the adherence of *C. albicans*. As many as four classes of adhesin-receptor interactions (protein-protein, protein-carbohydrate, carbohydrate-carbohydrate, and protein-unknown cell receptor hydrophobic interactions) have been suggested (4, 9). Our studies using equilibrium analysis of binding of *C. albicans* to human BECs suggested that at least three classes of adhesin-receptor interactions can be resolved (64). Some of the different receptors that have been shown to interact with *C. albicans* include both Arg-Gly-Asp (RGD)-containing glycoproteins (36, 40) and fucosyl- or *N*-acetylglucosamine-containing glycoproteins (8). Recently, Jimenez-Lucho et al. (26) suggested that *C. albicans* and other fungi bound specifically to the glycosphingolipid (GSL) lactosylceramide (LCS).

We have described the purification and initial characterization of a fimbrial adhesin from *C. albicans* yeast (66). The fimbrial preparation was obtained by very gentle homogenization protocols followed by size exclusion high-performance liquid chromatography. The filamentous structures were observable by electron microscopy, and the purity was assessed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. The major structural fimbrial subunit has a molecular mass of 66,000 Da and consists of ~85% carbohydrate (mainly mannose residues) and ~15% protein. The fimbriae bind directly to BECs and inhibit *C. albicans* binding to BECs (66). In this paper, we extended the findings of Jimenez-Lucho et al. (26) and show that *C. albicans* binds to other GSLs and that these GSLs were able to inhibit fimbrial binding to BECs. The binding of *C. albicans* fimbriae to BECs could also be inhibited by the synthetic disaccharide βGalNAc(1-4)βGal.

(Parts of these data were presented at the ASM Conference on Candida and Candidiasis: Biology, Pathogenesis, and Management, 25 to 28 March 1993, Baltimore, Md.)

## MATERIALS AND METHODS

**Purification of *C. albicans* fimbriae.** Fimbriae were purified from *C. albicans* 40 (a clinical isolate) as described by Yu et al. (66).

**Protein concentration determination.** A bicinchoninic acid protein assay (Pierce Chemicals) described by Smith et al. (62)

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was used to determine the concentration of fimbriae. Bovine serum albumin (BSA) was employed as a protein standard.

**Binding assays using TLC.** The thin-layer chromatography (TLC) plate binding assay was performed as described by Baker et al. (1) with minor modifications. Aluminum-backed silica gel Si60 high-performance TLC plates (Merck Kieselgel Si60; no fluorescence indicator; E. Merck, Darmstadt, Germany) were cut to produce plates (8 by 2.5 cm) which were chromatographed with 100% methanol to the top of the plate to remove impurities, and the plates were air dried. GSLs (10 μg of each) were loaded 1.0 cm above the base of the plate. The following GSLs purchased from Sigma Chemical Co. (St. Louis, Mo.) were used: monosialoganglioside (M-$GM_1$), asialoganglioside $GM_1$ (asialo-$GM_1$), asialoganglioside $GM_2$ (asialo-$GM_2$), LCS, and ceramide trihexoside (CTH). GSLs were separated on the TLC plates in chloroform-methanol-water (65:35:8, vol/vol/vol) and air dried. One set of plates was sprayed with 10% sulfuric acid in ethanol and heated at 100 to 150°C for 5 to 10 min to char the GSLs for visual detection, and the other set was used for the fimbrial binding assay. The four corners of the plate were bent to 90°, and the remainder of the assay was done with the TLC plates inverted in all solutions and at room temperature in an incubator shaker (model G25 Gyrotoryshaker; New Brunswick Scientific, New Brunswick, N.J.) at 20-rpm agitation. The TLC plate was blocked with 50 mM Tris (pH 7.5) containing 150 mM NaCl (TBS), 0.25% (wt/vol) gelatin, 3% (wt/vol) BSA, 5 mM EDTA, and 0.05% (vol/vol) Nonidet P-40 in a glass petri dish for 2 h at room temperature. The blocking solution was aspirated, and 10 ml of enriched fimbriae (EF) (100 μg of EF per ml in 100 mM TBS, pH 7.5) was then added. The fimbriae were allowed to bind to GSLs for 2 h at room temperature. The plates were gently washed (two times for 5 min each) with 10 ml of 100 mM TBS containing 0.1% (vol/vol) Tween 20 (TBST). The murine anti-EF monoclonal antibody Fm16 was diluted 1:200 with TBST, and 10 ml was added to the TLC plates. The solution was incubated for 1 h at room temperature. Unbound antibodies were removed by washing the plates with 10 ml of TBST (two times for 5 min each). The plate was then incubated with 10 ml of goat anti-mouse immunoglobulin G (IgG)–alkaline phosphatase conjugate (Jackson Laboratories) diluted 1:5,000 with TBST for 1 h at room temperature. The plates were washed (two times for 5 min each) with 10 ml of TBST. The alkaline phosphatase activity was localized with nitroblue tetrazolium chloride and 5-bromo-4-chloro-3-indolylphosphate (BCIP) dissolved in 100 mM Tris buffer, pH 9.5, containing 100 mM NaCl and 5 mM $MgCl_2$. Color development was quenched by rinsing the TLC plate with deionized water and submerging the plate into a 150 mM EDTA solution (pH 8.0) for 3 to 5 min. The plates were air dried and stored in plastic in the dark until they were photographed.

**Binding of *C. albicans* fimbriae to GSLs.** Polystyrene microtiter plates (Nunc) were coated with asialo-$GM_1$ and CTH (Sigma). Aliquots of the GSLs (5 μg/ml suspended in methanol) were added into the wells (100 μl per well), and the plates were incubated overnight at 4°C. The wells were washed three times with 250 μl per well of 10 mM phosphate-buffered saline (pH 7.4) containing 150 mM NaCl (PBS) supplemented with 0.05% (wt/vol) BSA (buffer A). Excess binding sites were blocked by the addition of 200 μl of 5% (wt/vol) BSA in PBS (pH 7.4) per well and incubation at 37°C for 1 h. Wells were washed three times with 250 μl of buffer A per well. EF ranging from 0 to 40 μg of protein per ml in buffer A were added to the wells (100 μl per well) and incubated for 2 h at 37°C. Aliquots of mouse anti-EF monoclonal antibody Fm16 (diluted 1:500) were added to each well (100 μl) and incubated at 37°C for 2 h. Wells were washed five times with 250 μl of buffer A per well. Antibody binding to EF was assessed by the addition of a goat anti-mouse heavy- and light-chain IgG–peroxidase conjugates (Jackson Laboratories) to each well (100 μl per well) and incubation for 1 h at 37°C. The wells were washed five times with 250 μl of buffer A per well, and a substrate solution containing 1 mM 2,2′-azido-di-(3-ethylbenzthiazoline sulfonic acid) (ABTS) in 10 mM sodium citrate buffer (pH 4.2) containing 0.03% (vol/vol) hydrogen peroxide was added (125 μl per well). The reaction was stopped by an addition of 125 μl of 4 mM sodium azide per well, and the $A_{405}$ was recorded.

**Inhibition of *C. albicans* fimbrial binding to immobilized GSLs.** The protocol for the assay of fimbrial binding to immobilized GSLs was similar to that employed for the assessment of *C. albicans* fimbrial binding to GSLs except that *C. albicans* fimbriae were preincubated with asialo-$GM_1$ and CTH for 1 h at 37°C prior to their addition into the wells. A fixed concentration of EF (50 μg/ml) was incubated with various GSL concentrations (0 to 15 μg/ml) in these assays. The remaining protocols were as described above for the direct binding assays.

**Binding of *C. albicans* fimbriae to synthetic βGalNAc(1-4)βGal.** βGalNAc(1-4)βGal-O$(CH_2)_8COOCH_3$ was synthesized by the method of Sabesan and Lemieux (57) and conjugated to BSA. The coupling ratio of disaccharide to BSA was 12:1. The protocol utilized for this assay was similar to that employed for the assessment of *C. albicans* fimbrial binding to GSLs except that the plates were coated with, per well, 100 μl of a 10-μg/ml solution of synthetic βGalNAc(1-4)βGal–BSA conjugate in 0.01 M carbonate buffer, pH 9.5. The remainder of the protocols were unchanged from those described above.

**Inhibition of *C. albicans* fimbrial binding to human BECs.** Human BECs were collected from 10 healthy, nonsmoking male volunteers and washed as described by Yu et al. (66).

Both GSLs (asialo-$GM_1$ and CTH) and βGalNAc(1-4)βGal–methylester were used to inhibit *C. albicans* fimbrial binding to BECs. The binding assay was performed using 12-μm-pore-size polycarbonate filter membranes (Nucleopore Costar Corp.) placed in chambers in a Manifold filtration apparatus equipped with individual vaccum stopcocks (model FH 225 V; Hoefer Scientific Instruments). The protocols of Yu et al. (66) were employed with some modifications. *C. albicans* fimbriae (50 μg) were preincubated with either βGalNAc(1-4)βGal–methylester, asialo-$GM_1$, or CTH (total volume of 1 ml of PBS, pH 7.2, containing 0.05% [vol/vol] Tween 20) at 37°C for 1 h. The mixtures were added to BECs ($2.0 \times 10^5$ BECs in 1 ml of PBS, pH 7.2) and incubated at room temperature for 1.5 h. The remaining protocols were as described by Yu et al. (66).

## RESULTS

**Binding of *C. albicans* fimbriae to GSLs on TLCs.** A number of glycolipids, separated on TLC plates, were examined for their ability to be recognized by fimbriae purified from *C. albicans*. Bound fimbriae on the TLC plates were visualized with a protein G affinity-purified anti-*C. albicans* fimbriae monoclonal antibody, Fm16, obtained from ascites tumors in BALB/c mice as previously described (66), and a goat anti-mouse IgG–alkaline phosphatase conjugate. Fm16 was produced by immunizing mice with *C. albicans* fimbriae and isolated from a hybridoma cell line that expressed IgG2a(κ) which bound to the fimbrial structural subunit. Fm16 was observed to bind to the cell surface of *C. albicans* and inhibit fimbria-mediated binding to human respiratory epithelial cells (66). Normal mouse IgG does not bind to *C. albicans* fimbriae.

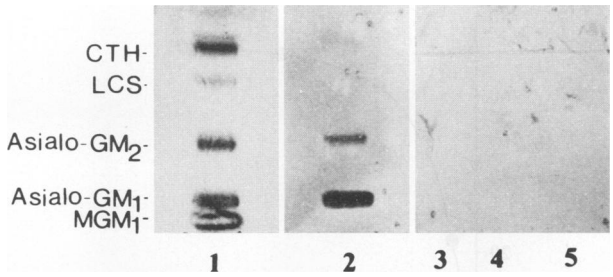


FIG. 1. Binding of *C. albicans* fimbriae to GSLs separated on TLC plates. GSLs (10μg) were chromatographed on TLC plates with a mobile phase of chloroform-methanol-water (65:35:8, vol/vol/vol). Lanes 1 and 2, charred GSL standards (CTH, LCS, asialo-$GM_2$, asialo-$GM_1$, and M-$GM_1$); lane 3, asialo-$GM_1$; lane 4, M-$GM_1$ and asialo-$GM_2$; lane 5, LCS and CTH. The TLC binding assay in which the GSLs were first incubated with *C. albicans* fimbriae is described in detail in the Materials and Methods. Fm16 was used to probe fimbrial binding in lane 2, while normal mouse IgG was used in lanes 3, 4, and 5 as a control. A goat anti-mouse IgG–alkaline phosphatase conjugate was utilized to detect bound fimbriae on the TLC plates. Color development was obtained with nitroblue tetrazolium chloride and BCIP dissolved in 100 mM Tris buffer, pH 9.5, containing 100 mM NaCl and 5 mM $MgCl_2$.

In this study, Fm16 was utilized to detect *C. albicans* fimbrial binding to TLC-separated GLCs and affinity-purified normal mouse IgG was employed as a control. The results in Fig. 1 showed that *C. albicans* fimbriae bound specifically to asialo-$GM_1$ [gangliotetraosylceramide: βGal(1-3)βGalNAc(1-4)βGal(1-4)βGlc(1-1)Cer] and asialo-$GM_2$ [gangliotriosylceramide: βGalNAc(1-4)βGal(1-4)βGlc(1-1)Cer]. A normal mouse IgG control instead of Fm16 failed to detect fimbrial binding to asialo-$GM_1$ and asialo-$GM_2$ (Fig. 1, lanes 3 and 4), as the normal mouse IgG does not bind to fimbriae. Fimbriae failed to bind to $GM_1$, LCS, or CTH [αGal(1-4)βGal(1-4)βGlc(1-1)Cer].

**Specificity of *C. albicans* fimbrial binding to GSL receptors.** The binding of *C. albicans* fimbriae to GSL receptors was ascertained with GSLs immobilized on microtiter plates. We used asialo-$GM_1$ and CTH (as a negative control) in solid-phase binding assays and found that *C. albicans* fimbriae bound to asialo-$GM_1$ in a saturable, concentration-dependent manner (Fig. 2A). The concentration of fimbrial protein required for half-maximal binding is 8 μg/ml under the assay conditions, indicating a reasonably high affinity of fimbriae for asialo-$GM_1$. Fimbriae failed to bind to CTH. The specificities of *C. albicans* fimbriae for GSLs were verified with competitive binding assays. GSLs were suspended in PBS at a sufficiently low concentration to prevent micellar formation. When homologous competitors were used in inhibition assays, *C. albicans* fimbrial binding to the respective immobilized asialo-$GM_1$ was reduced by 78% (Fig. 2B). As expected, no competition of fimbrial binding to CTH was observed, as fimbriae do not bind to this glycolipid (Fig. 2A). The concentration of asialo-$GM_1$ required for half-maximal inhibition is 1.44 μg/ml.

**Binding of *C. albicans* fimbriae to synthetic βGalNAc(1-4)βGal disaccharides.** Krivan et al. (41) have proposed that the minimal receptor structural requirement of a number of asialo-$GM_1$-specific adhesins is the disaccharide βGalNAc(1-4)βGal. This disaccharide sequence was synthesized and conjugated to BSA to determine if the *C. albicans* fimbriae would bind to this disaccharide. When βGalNAc(1-4)βGal–BSA conjugates were immobilized on microtiter plates, *C. albicans* fimbriae were observed to bind to these disaccharides in a saturable, concentration-dependent manner (data not shown). The interactions between fimbriae and the disaccharide were specific, as the binding of *C. albicans* fimbriae to the βGalNAc(1-4)βGal–BSA conjugates was competitively inhibited by solution-phase βGalNAc(1-4)βGal–methylester (Fig. 3A). The half-maximal inhibition was attained at 8.2 μM βGalNAc(1-4)βGal–methylester, suggesting a highly specific interaction. Furthermore, when asialo-$GM_1$ was employed as the competitor, the ganglioside also competitively inhibited *C. albicans* fimbrial binding to βGalNAc(1-4)βGal–BSA conjugates (Fig. 3B). The concentration of asialo-$GM_1$ required for half-maximal inhibition was 7.5 μg/ml.

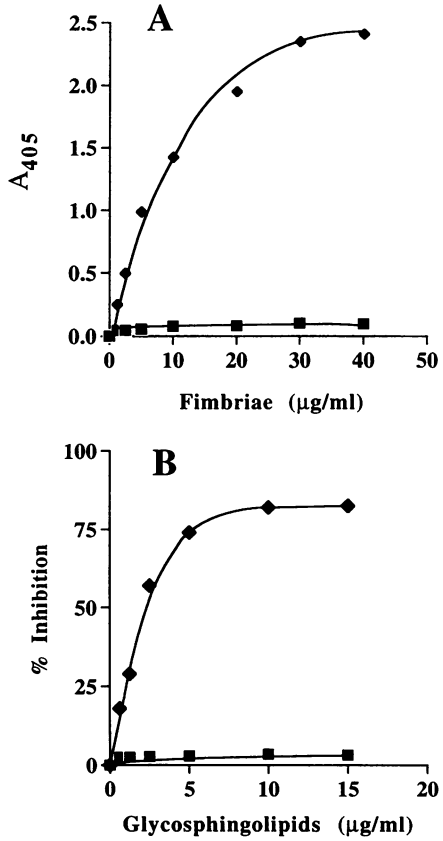


FIG. 2. Binding of *C. albicans* fimbrial adhesin to immobilized GSL receptors. (A) Binding of fimbriae to asialo-$GM_1$ (◆) and CTH (■) immobilized on microtiter wells (0.5 μg per well). The GSLs were incubated with EF (ranging from 0 to 4 μg per well) for an hour at 37°C. ELISA protocols utilizing anti-*C. albicans* fimbrial monoclonal antibody Fm16 as the primary antibody and a goat anti-mouse IgG–alkaline phosphatase conjugate as the secondary antibody were employed to quantitate fimbrial binding to asialo-$GM_1$ and CTH. The amount of fimbriae bound is represented as the $A_{405}$. (B) Inhibition of *C. albicans* fimbrial binding to asialo-$GM_1$ (◆) and CTH (■) with the respective homologous GSLs. The protocols were similar to those used for panel A except that the *C. albicans* fimbriae were preincubated with asialo-$GM_1$ and CTH at 37°C for an hour prior to their addition to the precoated microtiter wells. The percent inhibition is the inhibition of fimbrial binding in the presence of the competing antigens with respect to the binding in the absence of any competitors under identical conditions.

***C. albicans* fimbriae bind to GSL receptors on human BECs.** We have previously shown that the fimbriae of *C. albicans* are able to bind to BECs (66). Purified fimbriae were able to block *C. albicans* whole-cell binding to BECs (66). The receptors

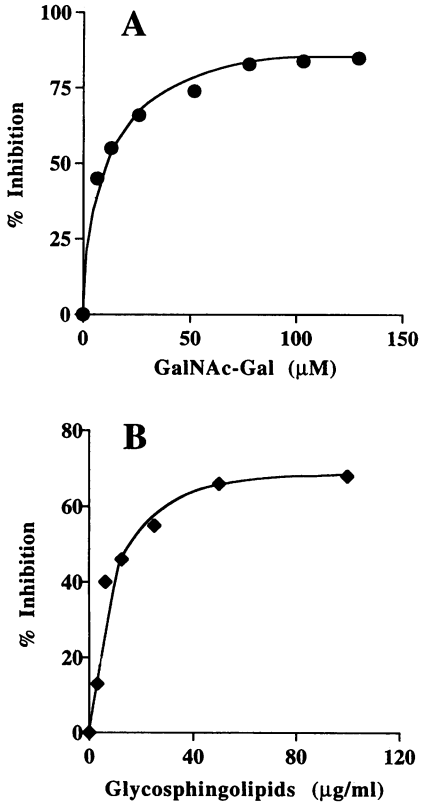


FIG. 3. *C. albicans* fimbrial adhesin binds to the minimal disaccharide sequence of βGalNAc(1-4)βGal. (A) Inhibition of fimbrial binding to βGalNAc(1-4)βGal–BSA conjugate. βGalNAc(1-4)βGal–BSA conjugate was immobilized onto microtiter wells (0.5 μg per well). These conjugates were incubated with EF that were preincubated with various concentrations of βGalNAc(1-4)βGal–methylester. The binding of fimbriae to the disaccharide conjugates was quantitated by the same ELISA protocols used for Fig. 2. (B) Inhibition of fimbrial binding to βGalNAc(1-4)βGal–BSA with asialo-$GM_1$. The conditions for these inhibition assays are similar to those used for panel A. The percent inhibition is the inhibition of fimbrial binding in the presence of the competing antigens with respect to the binding in the absence of any competitors under identical conditions.

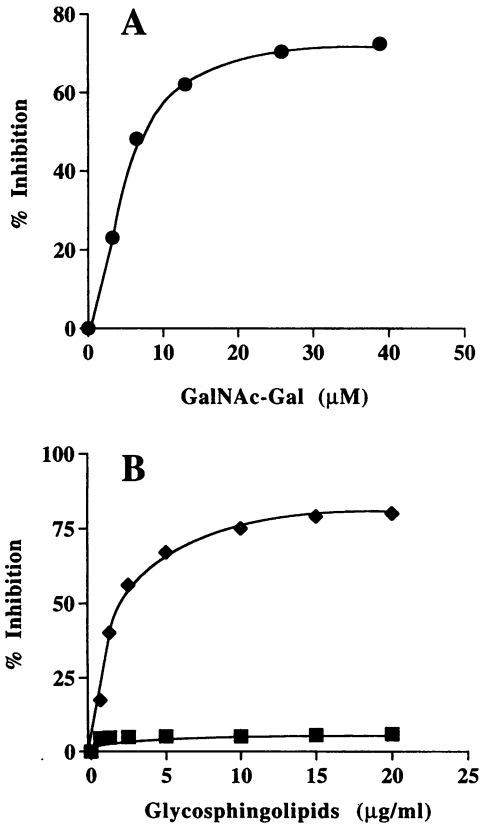


FIG. 4. Inhibition of *C. albicans* fimbrial binding to glycoconjugate receptors on human BECs with synthetic βGalNAc(1-4)βGal–methylester (A) and GSLs (B). BECs were collected from nonsmoking healthy male volunteers as described in Materials and Methods. These assays were performed using a Manifold filtration apparatus equipped with individual vacuum stopcocks (model FH 225V; Hoefer Scientific Instruments). The assay mixture consisted of $2.0 \times 10^5$ BECs, fimbriae (50 μg), and various concentrations of competitors in a total volume of 1.0 ml of 10 mM phosphate buffer, pH 7.2, containing 150 mM NaCl. *C. albicans* fimbriae were preincubated with either βGalNAc(1-4)βGal–methylester (●), asialo-$GM_1$ (◆), or CTH (■) for an hour at 37°C prior to addition to the BECs. The percent inhibition is the inhibition of binding in the presence of the competing antigens with respect to the binding in the absence of any competitors.

which mediated the binding to *Candida* fimbriae were not identified. In these experiments, fimbriae were preincubated with βGalNAc(1-4)βGal–methylesters, asialo-$GM_1$, or CTH prior to their addition to BECs. The results showed that βGalNAc(1-4)βGal–methylester (Fig.4A) and asialo-$GM_1$ (Fig. 4B) inhibited *C. albicans* fimbrial binding to BECs by 70 and 80%, respectively, suggesting that glycoconjugates present on the cell surfaces were interacting with fimbriae. CTH failed to inhibit *C. albicans* fimbrial binding to BECs.

## DISCUSSION

*C. albicans* is an opportunistic fungal pathogen that appears to be able to employ several adhesins to mediate attachment of the organism to cell surface receptors (4, 9). We have established that *C. albicans* produces a fimbrial adhesin which can mediate the adherence of the organism to exfoliated human BECs in in vitro binding assays (66). Fungal fimbriae have been previously described in other yeasts (16, 17, 52), and the *C. albicans* fimbriae appear to be similar to those structures. Fimbria-mediated adherence of bacterial organisms is a common theme, but such an adherence mechanism has not been described in yeasts (15, 25, 50, 61).

There has been a tremendous amount of literature supporting the role of carbohydrate receptors on glycolipids or glycoproteins in mediating attachment to bacterial adhesins (27, 41, 43). The initial observation of *C. albicans* binding to glycolipid receptors were made by Jimenez-Lucho et al. (26). We report here that *C. albicans* can utilize GSLs as receptors and that the yeast expresses fimbrial structures which mediate this interaction. *C. albicans* fimbriae bound specifically to asialo-$GM_1$ and asialo-$GM_2$ (Fig. 1 and 2). Synthetic disaccharides with the βGalNAc(1-4)βGal sequence found on the carbohydrate moiety of these gangliosides were sufficient for interaction with the *C. albicans* fimbriae (Fig. 3A and unpublished data). This interaction could be inhibited by asialo-$GM_1$ (Fig. 3B). We have previously demonstrated that *C. albicans* fimbriae bind to BECs and the fimbriae inhibit yeast binding to BECs (66). In these present studies, we showed that synthetic βGalNAc(1-4)βGal and asialo-$GM_1$ inhibited *C. albicans* fimbrial binding

to BECs (Fig. 4), suggesting that there are glycoconjugates present on BECs that could interact specifically with fimbriae. Significantly, the ability of the synthetic disaccharide to inhibit fimbrial binding to BEC receptors indicates that the receptors likely contain a βGalNAc(1-4)βGal sequence. These observations support the hypothesis that the minimal carbohydrate sequence required for binding of microorganisms to similar series of gangliosides is a βGalNAc(1-4)βGal sequence (41).

Unlike the findings of Jimenez-Lucho et al. (26) that described the binding of *C. albicans* to the GSL LCS, our data indicate that *C. albicans* fimbriae bind to asialo-$GM_1$. *C. albicans* 40, a clinical isolate used in the preparation of fimbriae in these studies, was different from the strain employed by Jimenez-Lucho et al. (26). Our culture and study conditions also differed from those employed by Jimenez-Lucho et al. (26). Thus, the two strains may express different adhesins requiring distinct receptors. In addition, the binding assay conditions used were also different. In our assays, 0.05% (vol/vol) Tween 20 was present in the buffers. We have observed that the absence of detergent in the buffers resulted in nonspecific binding to LCS as well as M-$GM_1$ and phospholipids (unpublished observations). The significance of this observation is unknown.

In these studies, we have identified an adhesin for *C. albicans* that recognized GSL receptors on BEC surfaces. We have not investigated whether the fimbrial adhesin is expressed in the mycelial form. Immunological data suggest that fimbriae are widely distributed among strains of *C. albicans* (unpublished observations). The fimbrial adhesin appears to differ from previously reported adhesins because of its receptor specificity (4, 5, 10, 20, 37, 65). We are attempting the isolation and purification of *C. albicans* fimbrial receptors from epithelial cells to determine whether GSLs represent in situ receptors with biological relevance to yeast adherence. Work is in progress in mouse infection models to evaluate the role of fimbriae in *C. albicans* virulence.

## ACKNOWLEDGMENTS

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