

ORIGINAL ARTICLE

CD101, a novel echinocandin with exceptional stability properties and enhanced aqueous solubility

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The echinocandins are an important class of antifungal agents. However, instability and, in some cases, lack of solubility have restricted their use to situations in which daily infusions are acceptable. CD101 is a novel echinocandin in development for topical and weekly i.v. administration that exhibits prolonged stability in plasma and aqueous solutions up to 40 °C. After incubation for 44 h in rat, dog, monkey and human plasma at 37 °C, the percent of CD101 remaining (91%, 79%, 94% and 93%, respectively) was consistently greater than that of anidulafungin (7%, 15%, 14% and 7%, respectively). Similarly, after incubation in phosphate-buffered saline at 37 °C, the CD101 remaining (96%) was greater than that of anidulafungin (42%). CD101 exhibited <2% degradation after long-term storage at 40 °C as a lyophilized powder (9 months) and at room temperature in 5% dextrose (15 months), 0.9% saline (12 months) and sterile water (18 months). Degradation was <7% at 40 °C in acetate and lactate buffers (6 to 9 months at pH 4.5–5.5). The chemical stability and solubility of CD101 contribute to dosing, pharmacokinetic, formulation and safety advantages over other echinocandins and should expand utility beyond daily i.v. therapy.

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INTRODUCTION

Candida is the leading cause of bloodstream infections within US hospitals and has been found to account for 22% of inpatient bloodstream infections.¹ Since the introduction of caspofungin in 2001, the echinocandins have become increasingly important in the treatment of these life-threatening fungal infections. Since 2009, echinocandins have been recommended as first-line therapy against suspected or confirmed candidemia and invasive *Candida* infections.^{2,3} As potent noncompetitive inhibitors of the plasma membrane-bound β -1,3-D-glucan synthase, the echinocandins inhibit the synthesis of β -1,3-D-glucan, a structural polymer that comprises up to 60% of the cell wall of *Candida* spp.⁴ The prevalence of this polymer in certain fungi, the lack of it in mammals, the low incidence of resistance and virtually nonexistent drug interactions make the echinocandins very attractive and the safest of all existing classes of systemic antifungal agents. Despite these advantages, the pharmacokinetic and stability properties of the currently approved echinocandins impose limitations on their use. Because of short half-lives and poor oral absorption, they were each developed for once-daily administration by i.v. infusion. Their stability necessitates that the i.v. dosing preparations be used within 24 to 48 h^{5–7} and precludes the introduction of other dosage forms, such as topical and s.c. preparations. Consequently, the echinocandins presently are used sparingly for indications in which daily infusion of the drug is impractical. In short, the susceptibility to hydrolytic, thermal and (for micafungin) photodegradation⁷ of the approved echinocandins impose limitations for manufacturing,

storage, usage and acceptable dosage forms for this otherwise attractive drug class.

A novel echinocandin, CD101 acetate (CD101; Figure 1), is presently being developed as a once-weekly i.v. formulation for the treatment and prevention of invasive fungal infections and also as a topical formulation for acute and recurrent vulvovaginal candidiasis. Characteristic of the echinocandins, CD101 is a cyclic hexapeptide with a lipophilic tail. It displays potency and spectrum of activity *in vitro* typical of the echinocandins.^{8,9} However, it has a distinct structural feature that confers much greater stability, leading to an exceptionally longer half-life^{10–12} and an improved safety profile.¹³ In this study, we present thermal and solution stability data for CD101 as a lyophilized powder and in various solutions, including prototype i.v. solutions. Solubility data are also presented. The stability and solubility features of CD101 not only provide advantages for manufacturing and storage, but also enable expansion of echinocandin use to include weekly i.v. infusions and topical and s.c. dosage forms.

MATERIALS AND METHODS

General

Unless otherwise indicated, all reagents were purchased from Sigma-Aldrich (St Louis, MO, USA). All solvents and modifiers were HPLC grade. HPLC analyses were performed using an Agilent 1200 Series LC with an autosampler, thermostatted column compartment and multi-wavelength detector. HPLC columns were purchased from Agilent (Santa Clara, CA, USA). Anidulafungin

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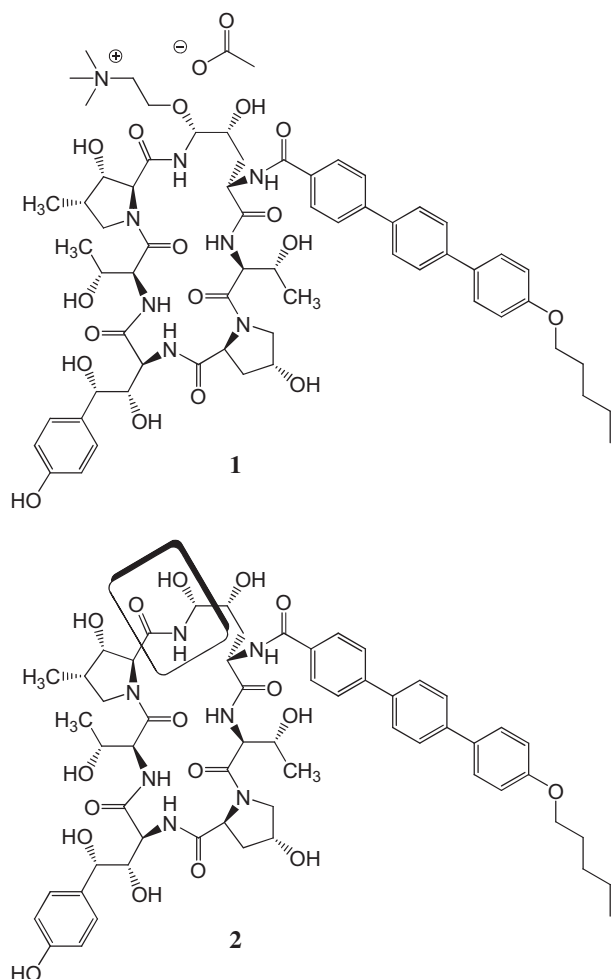


Figure 1 Structures of CD101 (1) and anidulafungin (2). The primary means of elimination *in vivo* for anidulafungin is chemical degradation that occurs initially at the hemiaminal region shown in the box. For CD101, the hemiaminal is replaced with a choline aminal ether that imparts greater stability and solubility to the product compound.

was obtained after isolation from commercial Eraxis (Pfizer, New York, NY, USA). The synthesis of CD101 will be described elsewhere.

HPLC analyses

All quantitative assays and purity assessments were performed using two reversed-phase HPLC methods. Method 1 was used to assess the purity of CD101 and to identify the formation of any degradation products. Method 2 was used to assess stereochemical stability at the hemiaminal ether position by separating the α -isomer (CD101, Figure 1) from any potential β -isomer, which has the opposite stereochemistry at the site of choline ether attachment. Quantitation was performed by comparison of peak areas of test samples to the peak areas of external reference standards, analyzed in separate HPLC injections within the same set of samples. The reference standards for these studies were solutions of known concentration of previously purified and characterized lots of anidulafungin and CD101.

Method 1. An Agilent Pursuit XRs Diphenyl column (4.6 mm i.d. \times 250 mm length, 3.0 μ m particle size) was used. Elution was performed with a column temperature of 40 °C and a gradient system with a flow rate of 1 ml min⁻¹ (A: H₂O with 0.1% TFA; B: acetonitrile with 0.1% TFA; %B: 10–42 over 5 min, 42–50 over 20 min). UV detection was performed at 300 nm.

Method 2. An Agilent Zorbax 300SB C3 column (4.6 mm i.d. \times 150 mm length, 3.5 μ m particle size) was used. Elution was performed with a column temperature of 60 °C and an isocratic system with a flow rate of 0.5 ml min⁻¹ (A: H₂O with 0.3% phosphoric acid; B: methanol with 0.3% phosphoric acid; 50% B over 40 min). UV detection was performed at 300 nm.

Stability in plasma and PBS buffer

Stock solutions of CD101 and anidulafungin were prepared in DMSO at concentrations of 1.0 mg ml⁻¹. Blank plasma (rat, dog, monkey, and human) was mixed with 10% volume of sodium phosphate buffer (1.0 M, pH = 7.4). In the control, phosphate-buffered saline (PBS, pH = 7.4) was used in place of plasma. Each respective matrix was mixed separately with 1.0% of the stock solutions of the test articles, bringing the starting concentration of analyte in each sample to \sim 10 μ g ml⁻¹. The sample volume for each solution was 5.0 ml. Each stability sample was divided into aliquots of 500 μ l that were incubated at 37 °C. At each stability time point (1, 2, 8, 21 and 44 h), an aliquot was quenched with acetonitrile (500 μ l, with internal standard) and centrifuged. The supernatant (100 μ l) was removed and analyzed by reversed-phase HPLC using Method 1.

Stability as a lyophilized powder

Samples from three lots of CD101 (lyophilized powder) were stored in clear borosilicate glass vials and sealed with polypropylene caps with Teflon liners at 40 °C for 6–9 months. No stabilizers or other excipients were added to the lyophilisate. Stability was monitored over a period of 9 months using reversed-phase HPLC methods 1 and 2. Appearance was also monitored.

Stability in i.v. infusion solutions

CD101 (3.33 mg ml⁻¹) in lactate buffer was diluted to 1.1 or 0.77 mg ml⁻¹ with 5% dextrose or 0.9% saline infusion solutions, respectively. The dextrose formulation solution was stored in an infusion bag at room temperature. The saline formulation solution was stored in a sealed, clear glass vial. Both were unprotected from light for up to 15 months. No stabilizers were added to the solutions. Stability was monitored using HPLC methods 1 and 2. The assay values were reported in comparison with a reference standard and are an indication of the amount of CD101 in solution. Values between 90 and 110% of the target concentration were considered to be within the specification. Appearance was also monitored.

Stability in aqueous solutions

CD101 stock solutions (acetate buffer, lactate buffer and USP sterile water) were made at concentrations of 3.33 mg ml⁻¹ and were stored in clear borosilicate glass vials sealed with polypropylene caps with Teflon liners. No stabilizers or other excipients were added. The lactate and some acetate-buffered solutions were incubated at 40 °C. The sterile water and some acetate-buffered solutions were kept at room temperature and unprotected from light. Stability was monitored up to 18 months using HPLC methods 1 and 2. The assay values were reported in comparison with a reference standard. Values between 90 and 110% of the target concentration (3.33 mg ml⁻¹) were considered to be within the specification. Appearance was also monitored.

Solubility studies

Accurately weighed CD101 (up to 25 mg) was dissolved in sterile water, ethanol and buffered solutions of acetate, citrate, lactate, tartrate, phosphate and Tris in clear glass vials to final volumes of 0.5 ml at room temperature. No solubilizers or other excipients were added. Stirring was performed up to 16 h as necessary to form a clear solution. Any sample that contained undissolved material was centrifuged for 5 min, and the supernatant was analyzed. The solution samples were analyzed by HPLC method 1.

RESULTS

Stability in plasma and PBS buffer

After incubation at 37 °C in rat, dog, monkey and human plasma, the percentage of CD101 remaining after 44 h was 91%, 79%, 94% and 93%, respectively. Stability of CD101 in PBS buffer was similar

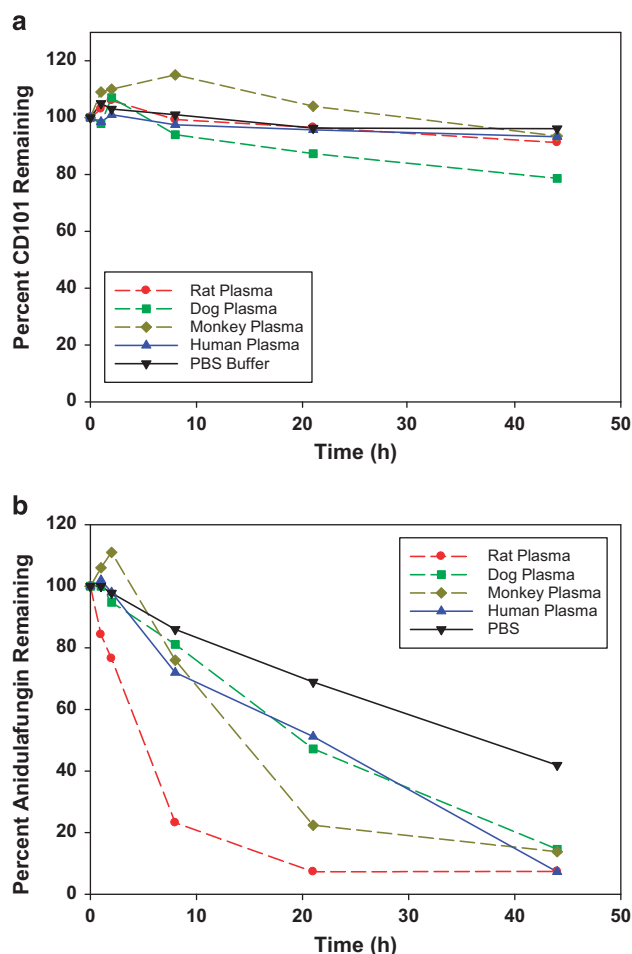


Figure 2 Degradation of CD101 (a) and anidulafungin (b) in plasma from different species and in phosphate-buffered saline (PBS) buffer. Each echinocandin ($10 \mu\text{g ml}^{-1}$) was incubated at 37°C for 44 h in plasma (rat, dog, monkey and human) and PBS buffer. Reactions were assayed at various time points (0, 1, 2, 8, 21 and 44 h) for the amount of intact echinocandin remaining, expressed as a percentage of the 0 h time point concentration. No stabilizers were used in the reactions. In contrast to anidulafungin, CD101 showed very little degradation in the matrices that were tested.

(96% remaining after 44 h). The time curves for CD101 in the various matrices are shown in Figure 2a. Degradation of anidulafungin was comparatively much faster in each of the four plasma matrices, as evidenced by nearly complete degradation of anidulafungin in <2 days. After incubation at 37°C in rat, dog, monkey and human plasma, the anidulafungin remaining after 44 h was 7%, 15%, 14% and 7%, respectively. These results were in good agreement with an earlier report demonstrating rapid chemical degradation of anidulafungin in human plasma.¹⁴ They are also consistent with a daily dosing regimen as described in the prescribing information.⁵ Degradation of anidulafungin was also extensive in PBS buffer (42% remaining after 44 h), although not as rapid as in the plasma experiments. The time curves for anidulafungin in the various matrices are shown in Figure 2b.

Stability as a lyophilized powder

The results from stability studies under accelerated conditions of two lots of CD101 lyophilisates are presented in Table 1. Values reported for individual lots are the percent area under the curve for CD101 and

Table 1 Stability data of CD101 as a lyophilized powder at 40°C

CD101 lot	Test	Time (months)				
		0	1	3	6	9
1	Chromatographic purity (% AUC)	99.0	98.6	98.4	98.3	96.5
1	Impurity and degradation products (% AUC)	1.0	1.4	1.6	1.7	3.5
2	Chromatographic purity (% AUC)	97.5	97.1	96.8	96.3	96.4
2	Impurity and degradation products (% AUC)	2.5	2.2	3.2	3.3	3.5
Average	Chromatographic purity (% AUC)	98.3	97.9	97.6	97.3	96.5
Average	Impurity and degradation products (% AUC)	1.8	1.8	2.4	2.5	3.5
Average	% Degradation	0	0.0	0.6	0.7	1.7

Abbreviation: AUC, area under the curve.

for the total of all impurities and degradation products. Averages for purity, impurity and degradation products and percent degradation are also presented. After storage at 40°C for 9 months in the absence of stabilizers, CD101 evidenced only a slight increase (~1.7%) in degradation products. The average chromatographic purity after 9 months was 96.5%. The emergence of a new peak indicating epimerization of the hemiaminal ether was not observed, suggesting no conversion from the α -isomer to β -isomer.

Stability of CD101 in i.v. infusion solutions

The results from stability studies of CD101 in two different i.v. infusion solutions (5% dextrose and 0.9% saline) are presented in Table 2. Purities are reported as the percent area under the curve for CD101 out of the total chromatogram. After storage at room temperature and exposure to light in the absence of stabilizers, CD101 exhibited no decrease in assay of active pharmaceutical ingredient in either the 5% dextrose solution after 15 months or in 0.9% saline solution after 12 months. Degradation was minimal in each solution over the course of the study. In addition, the emergence of a new peak indicating epimerization of the hemiaminal ether was not observed, suggesting no conversion from the α -isomer to β -isomer.

Stability of CD101 in aqueous solutions

The results from stability studies of CD101 in different aqueous solutions at varying pH in the absence of stabilizers are presented in Table 3. Purities are reported as the percent area under the curve for CD101 out of the total chromatogram. Degradation was slow under accelerated conditions (40°C) over a period of 6 to 9 months in slightly acidic buffered solutions. CD101 displayed <7% and 4% degradation in acetate buffers at pH 4.5 and 6.0, respectively. Degradation was <5% in lactate buffers (pH 4.5 and 5.5) over periods of 6 and 9 months, respectively, at 40°C . In contrast, degradation was extremely low at room temperature in acetate buffers (pH 4.5 to 6.0) and sterile water over 18 months. No epimerization of the hemiaminal ether was observed in any of the samples.

Solubility

The solubility of CD101 was evaluated in various aqueous solutions, buffered solutions (pH range from 4.5 to 9.5) and nonaqueous media. Anidulafungin was also evaluated under many of the same conditions. The solubility results are displayed in Table 4. CD101 showed excellent solubility ($>150 \text{ mg ml}^{-1}$) in sterile water, in stark contrast to the $<0.1 \text{ mg ml}^{-1}$ demonstrated by anidulafungin in the absence of

Table 2 Stability data of CD101 in i.v. infusion solutions

CD101 infusion solution	Concentration (mg ml ⁻¹)	Test	Time (months)						
			0	1	3	6	9	12	15
5% Dextrose	1.1	Assay (mg ml ⁻¹)	1.11	1.12	1.10	—	1.13	1.12	1.11
		Purity (% AUC)	97.3	97.1	97.2	—	98.1	96.9	97.7
0.9% Saline	0.77	Assay (mg ml ⁻¹)	0.80	0.81	0.79	0.82	0.83	0.79	—
		Purity (% AUC)	93.7	93.5	93.7	94.4	94.2	94.0	—

Abbreviation: AUC, area under the curve.

Table 3 Stability data of CD101 in aqueous solutions at varying pH

CD101 solution	Conc. (mg ml ⁻¹)	Temp (°C)	Test	Time (months)						
				0	1	3	6	9	12	18
Acetate buffer (20 mM, pH 4.5)	3.3	RT	Assay (mg ml ⁻¹)	3.25	3.26	3.16	3.32	3.62	3.70	3.60
			Purity (% AUC)	97.7	96.6	96.6	96.9	97.4	97.3	97.4
Acetate buffer (20 mM, pH 4.5)	3.33	40	Assay (mg ml ⁻¹)	3.28	3.24	3.14	3.25	—	—	—
			Purity (% AUC)	97.7	96.0	94.5	91.2	—	—	—
Lactate buffer (20 mM, pH 4.5)	3.33	40	Assay (mg ml ⁻¹)	3.18	3.21	3.11	3.20	3.16	—	—
			Purity (% AUC)	93.9	92.6	92.3	91.1	89.3	—	—
Lactate buffer (20 mM, pH 5.5)	3.33	40	Assay (mg ml ⁻¹)	3.32	3.42	3.21	3.41	3.18	—	—
			Purity (% AUC)	95.6	93.5	92.2	92.3	90.9	—	—
Acetate buffer (20 mM, pH 6.0)	3.33	RT	Assay (mg ml ⁻¹)	3.21	3.25	3.15	3.20	3.50	3.50	3.37
			Purity (% AUC)	97.4	96.7	96.6	96.0	97.6	97.5	97.6
Acetate buffer (20 mM, pH 6.0)	3.33	40	Assay (mg ml ⁻¹)	3.24	3.19	3.10	3.00	—	—	—
			Purity (% AUC)	97.4	95.9	95.6	93.8	—	—	—
Sterile water	3.33	RT	Assay (mg ml ⁻¹)	3.20	3.20	3.14	3.20	3.49	3.32	3.33
			Purity (% AUC)	97.3	96.6	96.7	96.1	96.7	97.4	97.4

Abbreviations: AUC, area under the curve; RT, room temperature.

solubilizers. CD101 also demonstrated high solubility (>45 mg ml⁻¹) in buffers made from acetate (pH 4.5 and 6.0), lactate (pH 6.0, 6.5, 7.4 and 8.5) and Tris (pH 7.4 and 8.5). Solubilities for CD101 were noticeably lower in phosphate and citrate buffers in comparison with the other media evaluated. Absent solubilizers, anidulafungin did not show solubility of >0.1 mg ml⁻¹ in any of the aqueous conditions tested. It did, however, show good solubility (>17 mg ml⁻¹) in ethanol, exceeding that observed for CD101 (14 mg ml⁻¹).

DISCUSSION

Stability in plasma

Chemical degradation marked by cleavage of the cyclic echinocandin core is common to the currently approved echinocandins and occurs in both plasma and buffered solutions, resulting in inactive degradants that are subject to further reaction and degradation.^{15–17} This pathway is a main mechanism of clearance *in vivo* for each of these therapeutics.¹⁴ In great contrast, CD101 is highly stable in plasma from various species and in PBS buffer. As illustrated in Figure 3, the ring-opening step that initiates the chemical degradation cascade of anidulafungin and other echinocandins is disfavored in CD101 because of the presence of the hemiaminal ether moiety. Whereas the hemiaminal hydroxyl of anidulafungin leads to a highly reactive, open-chain aldehyde, the corresponding step with the hemiaminal ether of CD101 would result in an oxonium ion, which is disfavored energetically. This explanation is further supported by prior work from Damle *et al.*¹⁴ regarding the stability of anidulafungin *in vitro* and *in vivo*. They found that anidulafungin undergoes rapid chemical

degradation in human plasma and PBS at 37 °C. The primary degradation product was itself reactive, undergoing further transformation. During *in vivo* studies utilizing a radioactive tag, they found that degradation products of anidulafungin persist in the body until eventual elimination in the feces. In our studies, formation of such a degradation product was not observed with CD101. We used anidulafungin as the comparator in these studies not only because of the structural similarity to CD101, but also because anidulafungin has the longest plasma half-life of the approved echinocandins across species.^{18–22} The unique chemical stability of CD101 has largely circumvented the main route of elimination (chemical degradation via ring opening) that is observed for anidulafungin and is likely a key contributor to the improved pharmacokinetics of CD101, although this alone may not entirely explain the long half-life that is observed *in vivo* across species (typically 3-fold to 5-fold longer than that of anidulafungin).¹⁰ In addition, the lack of degradation and the absence of open-chain aldehyde formation suggest that CD101 may offer higher margins of safety with fewer dose-limiting toxicities over echinocandins that generate such reactive degradants.¹³

Stability as a lyophilized powder

The stability of the CD101 lyophilisate, even at 40 °C in the absence of stabilizers (Table 1), is beneficial both for manufacturing of the active pharmaceutical ingredient and for enabling formulation of a stable drug product. In manufacturing, concerns of thermal stability between purification and formulation to the drug product are abated. It is also suggestive of a potentially long shelf-life without the need of

Table 4 Solubilities at room temperature for CD101 and anidulafungin in various solvent conditions

Solvent	Concentration (mg ml ⁻¹)	
	Anidulafungin	CD101
Sterile water	<0.1	> 150
10 mM acetate buffer, pH 4.5	ND	> 45
100 mM sodium acetate buffer, pH 6.0	ND	> 48
10 mM citrate buffer, pH 6.0	ND	~2
100 mM citrate buffer, pH 6.0	ND	~0.005–0.01
100 mM tartrate buffer, pH 6.0	ND	~0.018
100 mM lactate buffer, pH 6.0	ND	> 47
100 mM lactate buffer, pH 6.5	ND	> 45
10 mM phosphate buffer, pH 6.5	~0.001	> 29
100 mM phosphate buffer, pH 6.5	~0.001	~0.5
10 mM phosphate buffer, pH 7.0	~0.004	> 20
100 mM phosphate buffer, pH 7.0	~0.001	~0.006
10 mM phosphate buffer, pH 7.4	~0.004	~5
100 mM phosphate buffer, pH 7.4	~0.001	~0.006
100 mM Tris buffer, pH 7.4	ND	> 47
100 mM lactate buffer, pH 7.4	ND	> 51
100 mM Tris buffer, pH 8.5	ND	> 47
100 mM lactate buffer, pH 8.5	ND	> 52
10 mM phosphate buffer, pH 9.5	0.015	~7
100 mM phosphate buffer, pH 9.5	~0.002	~0.008
Saline (0.9%)	~0.001	~0.18
Saline (0.09%)	~0.005	> 1.4
Ethanol	> 17	14
Glycerol	1.5	> 23

Abbreviation: ND, not determined.

refrigeration and the minimization of loss because of short expiration dates; further studies to investigate this are underway. The increased stability of the active pharmaceutical ingredient without stabilizers has allowed development of a lyophilized formulation that is stable at room temperature and opens the door to other formulations, such as topical²³ and s.c.,²⁴ that are not viable with the currently approved echinocandins because of their insufficient stability.

Stability in i.v. infusion solutions

The stability of CD101 in infusion solutions was measured by assay and impurity profile. The former quantitatively measures the amount of CD101 remaining in solution over the course of the study. The latter provides information on levels of individual degradants arising via epimerization, hydrolysis or other mechanisms. As both the assay and the purity of CD101 remain unchanged over the course of the studies (Table 2), the results indicate that neither precipitation nor degradation occurred in the infusion bags up to 15 months in 5% dextrose or 12 months in 0.9% saline. These observations suggest that, unlike the currently approved echinocandins, infusion solutions of CD101 could be prepared without stabilizers and stored without concern of precipitation, degradation or photolysis.

Stability in aqueous solutions

CD101 showed minimal degradation at room temperature in water or acetate buffers (pH 4.5 and 6.0, Table 3). At 40 °C, degradation is noticeable by 1 month, becoming more evident at each time point thereafter. In general, drug was lost not to precipitation in these studies, but to formation of impurities at the higher temperatures. The

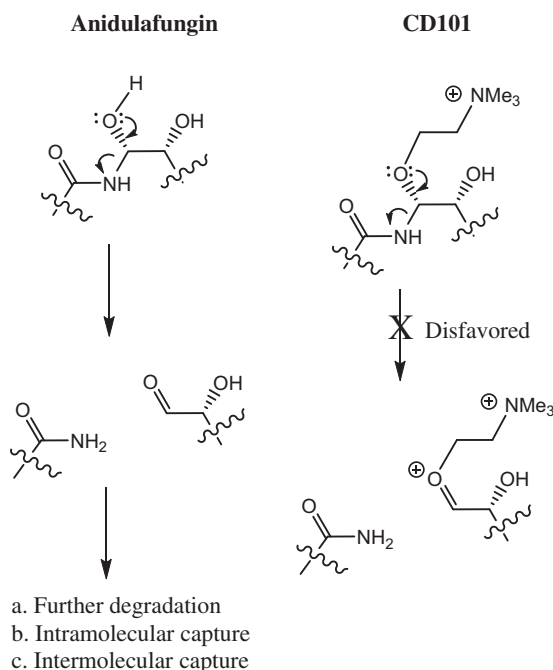


Figure 3 Proposed mechanism of the first step of the chemical degradation pathway for echinocandins at physiologic pH. The cyclic anidulafungin can undergo a ring-opening event in which the hemiaminal cleaves to form a linear peptide having a terminal amide and an aldehyde from the C5 hydroxyl of the ornithine residue. This open-chain degradant is then subject to further degradation. In addition, the reactive aldehyde that is generated is then available for covalent reaction intra- or intermolecularly. This pathway is disfavored for CD101, as the first step would result in an oxonium ion. This oxonium formation is likely further discouraged by the proximity of the quaternary ammonium cation of the choline.

results from acetate buffers (pH 4.5 and 6.0) at 40 °C suggest that lower pH may also accelerate the degradation of CD101, but more studies are needed to confirm this.

Solubility

In the absence of any solubilizers, CD101 showed exceptional solubility in sterile water. Although the solubility remained high in the presence of many buffering agents representing a broad pH range, the solubility was greatly diminished in some buffers. The monovalent carboxylic acid buffers (acetate and lactate) were good media for CD101, with solubility remaining high throughout the pH range and buffer concentrations tested. Similarly, the solubility was also high in the amine-based Tris buffer. These observations are in contrast to the diminished solubility in the polyvalent buffers (citrate and phosphate). The effect appears to be a function of the polyvalent acid component of the buffers rather than pH. At pH 7.4 and under the same buffer concentrations, CD101 solubility was very high in both Tris and lactate buffers, but very low in phosphate buffer. A similar observation was observed at pH 6.0, at which solubility was high in acetate and lactate buffers, but very low in citrate and phosphate buffers. The influence of the polyvalent acids on solubility is further supported by the consistent observation of higher solubility at lower concentrations of polyvalent acid buffers irrespective of pH.

The reason for the diminished solubility in the presence of polyvalent acidic buffers may be a result of ion exchange of the acetate counterion with the polyvalent acid and the potential for aggregation, but that is unclear at this time. Anidulafungin was

selected as the comparator because of the structural similarity to CD101. The choline substitution, while having negligible effect on the activity *in vitro*,^{7–8} made a profound effect on the solubility and stability properties of this echinocandin.

Conclusions

CD101 is a novel echinocandin with a choline moiety at the C5 ornithine residue of the cyclic echinocandin core. The structural modification affords an echinocandin with increased solubility and exceptional stability in plasma, in aqueous and buffered solutions, and as a lyophilized powder. The exceptional stability in plasma and lack of degradation products likely contribute to the long half-lives across species and increased safety observed for CD101. The stability and solubility properties of CD101 suggest benefits to manufacturing and storage as well as flexibility regarding i.v. preparation in pharmacies. These properties may also enable dosage forms new to echinocandins, such as topical, s.c. and fast i.v. push preparations.

CONFLICT OF INTEREST

KDJ, BRK and CPL have been consultants for and are stockholders of Cidara Therapeutics, the company developing CD101. AV is a stockholder of Cidara Therapeutics.

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