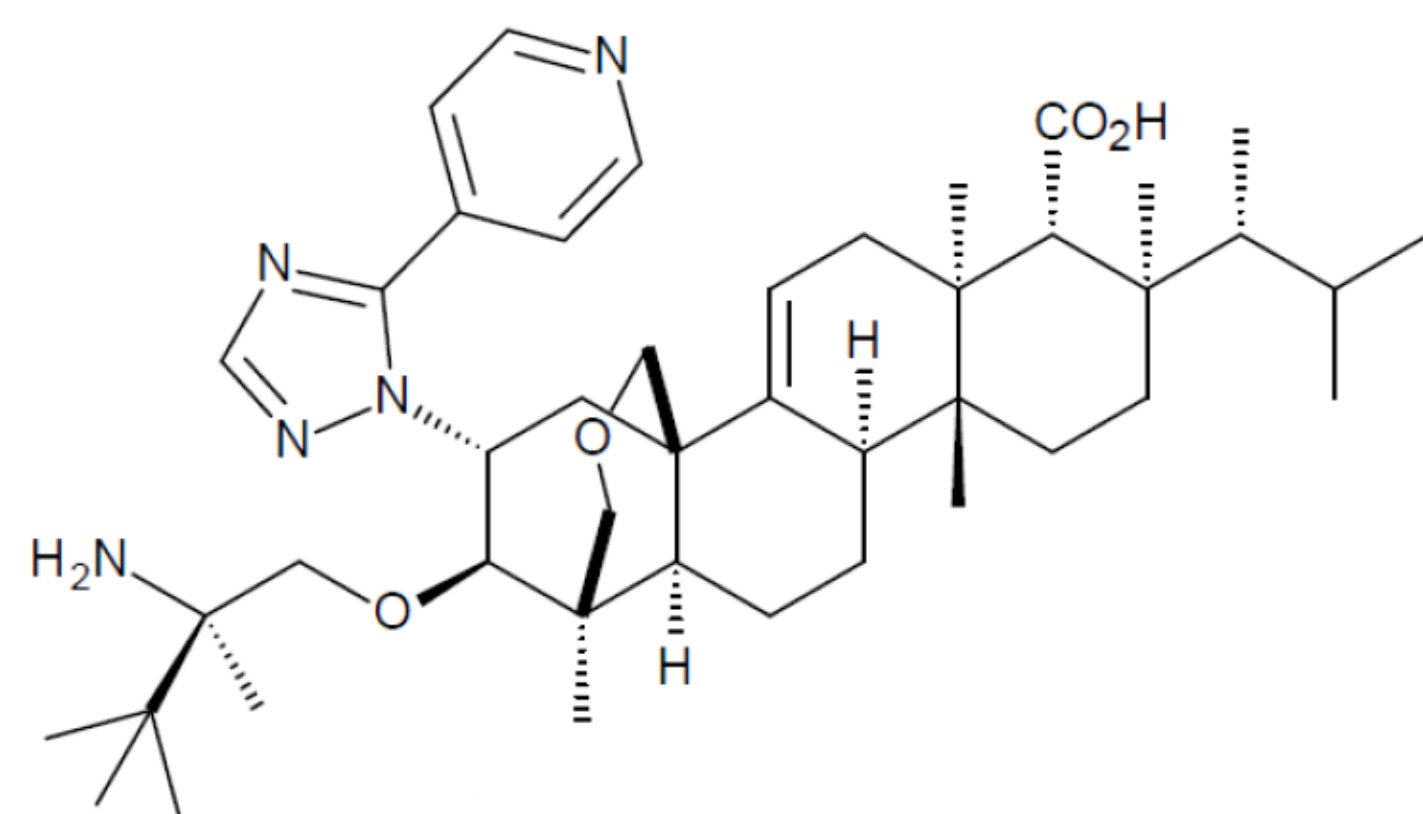


Vaginal Concentrations of SCY-078, a Novel Glucan Synthase Inhibitor, Following Oral Administration in Mice

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INTRODUCTION

- SCY-078 is an oral and intravenous semi-synthetic triterpenoid antifungal glucan synthase inhibitor, currently in development for the treatment of invasive and mucocutaneous fungal diseases



• C₆H₈O₇

- The ability of a pharmacologic agent to reach target organ(s) in therapeutically meaningful concentrations is one of the fundamental considerations when developing effective anti-infective treatments.

OBJECTIVE

To determine the exposure of SCY-078 in vaginal tissue and secretions, and the relationship to concentrations in plasma, following oral administration of SCY-078 to mice as a recognized model for *Candida* infections.

METHODS: STUDY DESIGN

Female CD-1 mice (n=3/time point/dose group) were given SCY-078 via oral gavage for either one, two or eight total doses ranging from 10 to 80 mg/kg, consisting of QD and BID dose regimens, with and without loading doses, according to the following table:

	Day 1	Days 2-4
QD (mg/kg)	10, 20, 40, 80	NA
BID (mg/kg)	10/5, 20/10, 40/20, 80/40	NA
BID (mg/kg)	10/5, 20/10, 40/20, 80/40	5/5, 10/10, 20/20, 40/40

Blood, vulvovaginal tissue and vaginal secretions were collected pre-dose, and at 1, 2, 4, 6, 8, 12, 18 and 24 hours post-dose, following the final dose administered per group. Samples were then processed, extracted via protein precipitation and analyzed for SCY-078 via LC MS/MS. A correction factor was determined based on urea content in vaginal lavage samples relative to plasma in order to calculate the concentration of SCY-078 in vaginal secretions.

RESULTS

Plasma pharmacokinetics (AUC₀₋₂₄), and vaginal tissue and secretion concentrations

Dose (mg/kg)	Plasma (µg*hr/ml)	Vaginal Secretion (µg*hr/ml)	Vaginal Tissue (µg*hr/ml)
QD			
10	8.33	1.32	26.7
20	19.7	1.87	53.6
40	42.3	4.41	187
80	75.5	12.3	171
BID			
10/5	7.47	1.55	24.6
20/10	16.6	4.21	72.9
40/20	46.5	10.6	204
80/40	101	17.8	337
BID repeat-dose			
10/5	5.12	4.32	24.4
20/10	14.6	8.63	71.6
40/20	53.0	38.8	275
80/40	143	120	1798

CONCLUSION

- Results show that following oral administration, SCY-078 levels in vaginal tissue exceed those observed in plasma confirmed its ability to readily distribute and accumulate in the vagina.
- Given SCY-078 fungicidal activity against *Candida* species along with its vaginal distribution, make it an attractive candidate for the treatment of vulvovaginal candidiasis.