Technical Report Summary: Microbiologic Testing

Flucytosine 500mg capsules (2 capsules) mixed with BASSA-GEL™ (DRUG) was tested against the identified pathogens and the results of these tests are reported as follows. Should there be only a "blue line" reported that means the DRUG was so effective against the pathogen that the detection limit was below the assay of the experiment.

Methods Overview

Methods for this laboratory study were adapted from Beardon *et al* and from FDA Docket No. FDA-1975-N-0012.[1, 2] All experiments were performed using the commercially available formulations. Reductions in bacterial counts between agents were determined.

Methods and Results

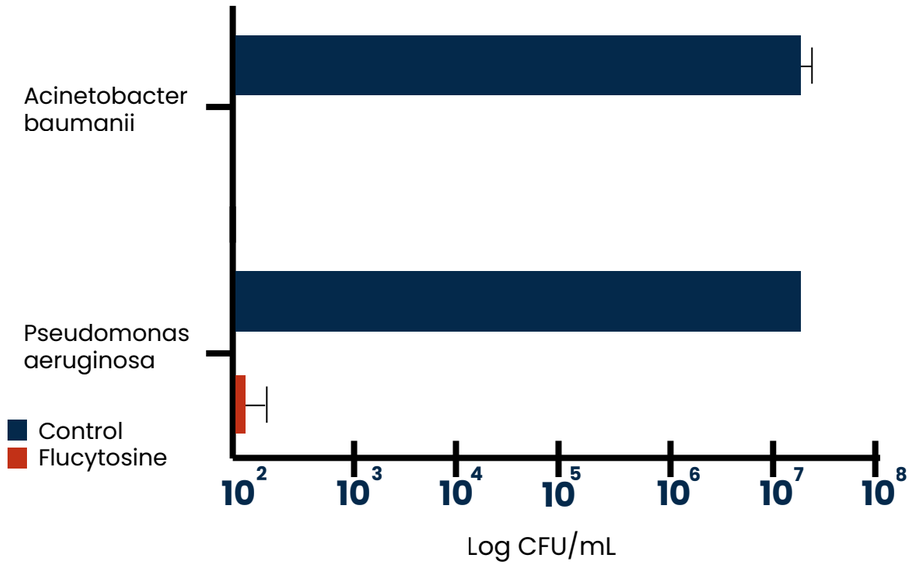
Tested organisms included[3, 4]

- Acinetobacter baumannii (ATCC BAA-747)
- Pseudomonas aeruginosa (ATCC 27853)

Antimicrobial agents: Flucytosine 500mg capsules (NDC 42494-0340-01) - 2 capsules mixed with BASSA-GEL™

Experiment

Pre-sterilized discs were saturated with 1 × $10^{7\text{-}8}$ CFU/mL bacterial cultures and incubated for 24 hours to model an *ex vivo* wound infection. Discs were then treated with the gel/drug solution or positive control (phosphate-buffered saline, PBS) and incubated aerobically at 37 °C for an additional 24 hours. Following incubation, discs were washed, serially diluted, and plated on blood agar for CFU/mL enumeration using the spread-plate technique. Results are reported as mean log CFU/mL ± standard error. As noted in the executive summary, a "blue line" indicates bacterial counts below the assay's limit of detection due to high drug efficacy.



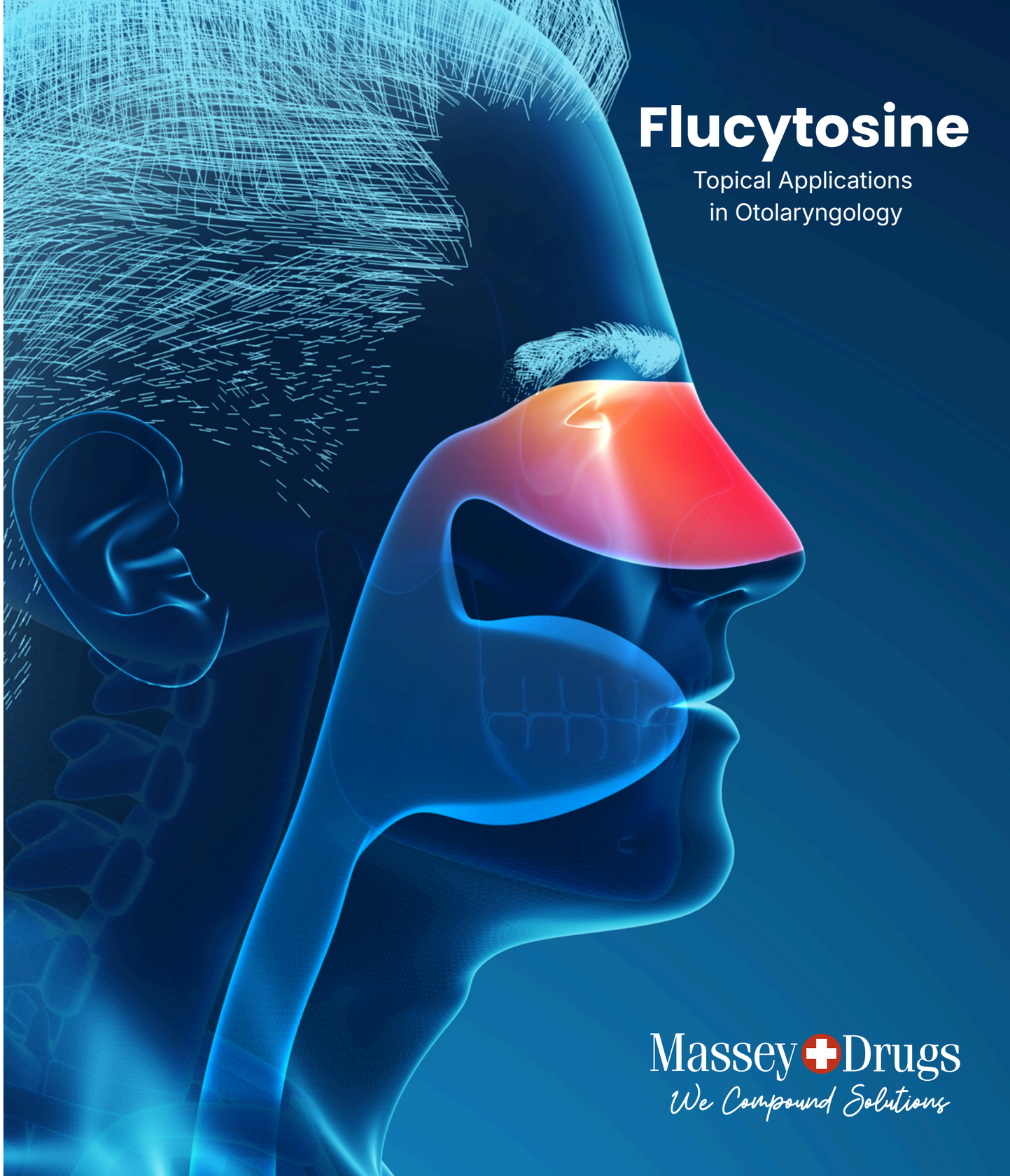
Interpretation

Flucytosine with BASSA-GEL™ was tested in a model mimicking a bandaged wound. The experiment demonstrated significant reductions in bacterial species tested.

References

1. Bearden DT, Allen GP, Christensen JM. Comparative in vitro activities of topical wound care products against community-associated MRSA. J Antimicrob Chemother. 2008;62:769-772.
2. Huang DB, Okhuysen PC, Jiang ZD, DuPont HL. Enteroaggregative E. coli. Am J Gastroenterol. 2004;99:383-389.
3. Rezzoagli C, et al. Repurposed drugs targeting iron uptake in Pseudomonas aeruginosa. Evol Med Public Health. 2018:246-259.
4. Imperi F, et al. Antivirulence fluoropyrimidine drugs in Pseudomonas aeruginosa. Front Cell Infect Microbiol. 2019;9:49.

Technical Report data derived from University of Houston Microbiology Research Laboratories.



Overview

Flucytosine was approved as an **oral antifungal drug** several decades ago. However, its clinical utility is limited in this capacity because of systemic toxicity concerns related to poor renal function and the need for high doses and frequency. In recent years, ENTs have been using flucytosine topically-specifically in **nasal irrigations**-for sinusitis with susceptible **fungal** and/or **gram-negative bacterial** etiology.

Topical administration allows for high drug concentrations at the target site with minimal systemic absorption.

How Flucytosine Works

Flucytosine is absorbed by fungus via the enzyme cytosine permease. Inside the fungal cell, the enzyme cytosine deaminase converts flucytosine to 5-FU allowing it to inhibit normal fungal RNA and DNA synthesis.

Although classified as an antifungal, in vitro models demonstrate activity against select gram-negative bacteria such as **Pseudomonas aeruginosa**, likely due to similar metabolic pathways.

Potential Clinical Applications (ENT)

Topical Flucytosine may be considered in the following settings:

- Sinusitis with fungus and/or gram-negative bacteria
- Patients unable to tolerate systemic treatments
- Microbial resistance to standard therapy
- Swish-and-spit oral rinses

Use is typically culture-directed and intended for localized application rather than systemic exposure.

Is This a Standard Treatment?

No. Topical application of commercial flucytosine capsules is considered off-label and the FDA does not review compounded versions for safety or efficacy. However:

- The mechanism of action is well established
- Laboratory data supports antimicrobial activity
- Topical dosing is substantially lower than systemic dosing
- Safety considerations are favorable with low systemic exposure
- Additional topical antimicrobials can be added to the treatment regimen

Topical flucytosine is a reasonable adjunct or alternative option for patients where conventional regimens are insufficient.

Safety Considerations

Systemic flucytosine use is associated with hematologic, hepatic, and renal toxicities

- These risks are dose-dependent and related to high plasma concentrations

Topical use safety considerations:

- Maximum topical exposure is 1000 mg/day and much lower than oral dosing - oral dosing for a 120-lb patient is 2,700–8,100 mg/day
- Minimal systemic absorption is expected
- Drug–drug interactions and renal concerns are generally avoided
- Caution remains appropriate in pregnancy if systemic exposure is anticipated

Prescribe Flucytosine

Drug/Strength/Form:
Flucytosine 500mg Capsule - #60

Price:
When covered by insurance, generic copay

Qty:
1 capsule/dose

Sig:
Irrigate with 1 capsule twice daily

1. Login to our **Practitioner Portal** at masseydrugs.com and download Rx form or call us at 833.540.3500.
2. Complete Rx form and FAX to: 800.637.2601.
3. We contact the patient to confirm address.
4. Medication ships to patient in 24-48 hours.

Compounded medications are available by prescription only.
The FDA does not evaluate compounded medications for safety or efficacy.

Questions?

Contact your Massey Drugs Medical Liaison or call 833.540.3500 to speak with a pharmacist.

Practitioner Portal

Massey Drugs

3501 Cloverdale Road • Florence, AL 35633
833.540.3500 • FAX 800.637.2601
masseydrugs.com • M-F • 8AM - 6PM CST

Licensed to serve patients in:
Alabama • Florida • Georgia • Tennessee • Mississippi • Illinois • Connecticut • Ohio • Texas
North Carolina • South Carolina • New York • Louisiana • Pennsylvania • Indiana • Kentucky

NABP Accredited Compounding Pharmacy