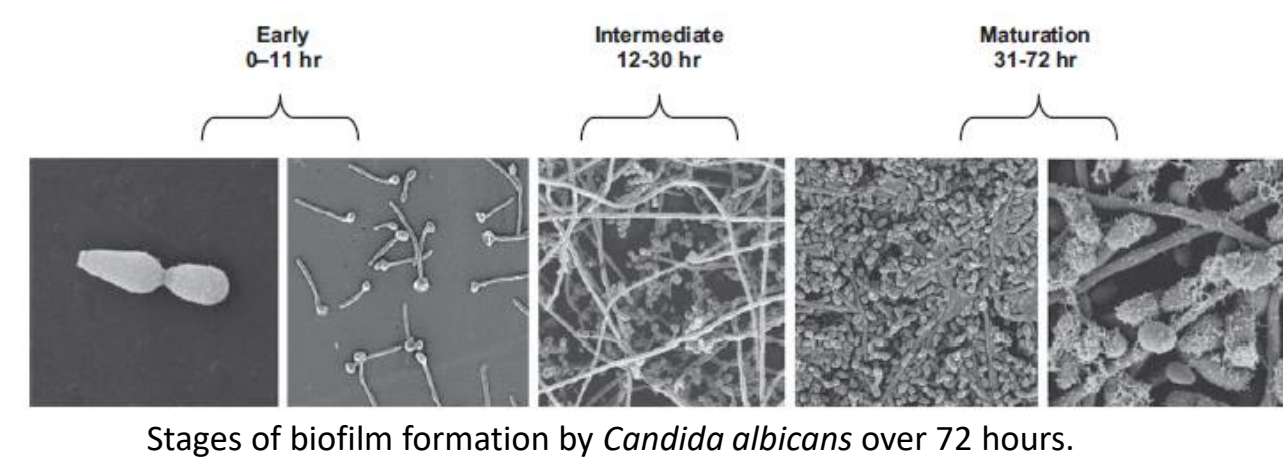


INTRODUCTION

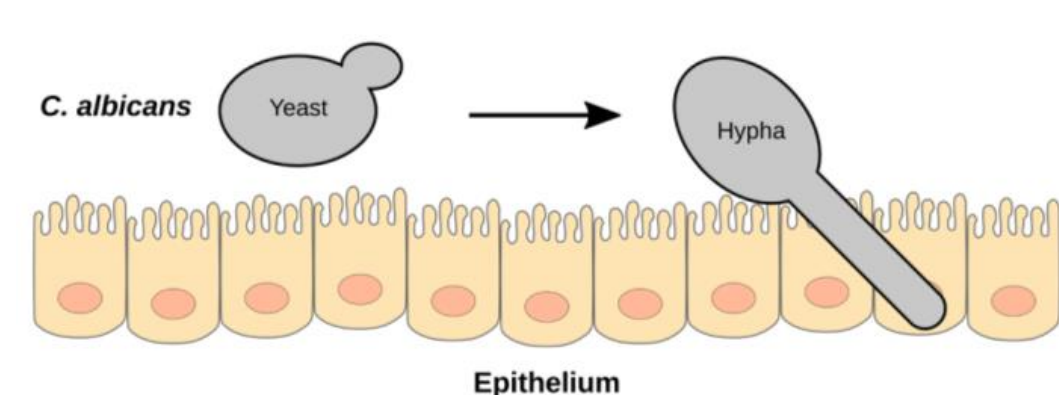
- Candida albicans* is a fungus capable of causing infections in immunocompromised individuals, as a result of HIV/AIDS, organ transplants, and chemotherapy.
- Candida* infections range from superficial infections, such as oral thrush, to life threatening systemic infections.
- Two factors that allow *Candida* to cause infections are biofilm formation and filamentation.
- Biofilms are complex communities of cells attached to biotic or abiotic (medical implant devices) surfaces and are resistant to antifungal drugs, like fluconazole.
- Currently amphotericin B is the only drug effective against biofilms; however, it is highly toxic to humans.
- Filamentation is the transition from yeast to hyphae and is essential for fungal invasion of host tissues.
- The purpose of this project was to test statins, FDA approved drugs for lowering cholesterol, for their ability to inhibit biofilm formation and filamentation.



Oral thrush caused by *Candida albicans*.



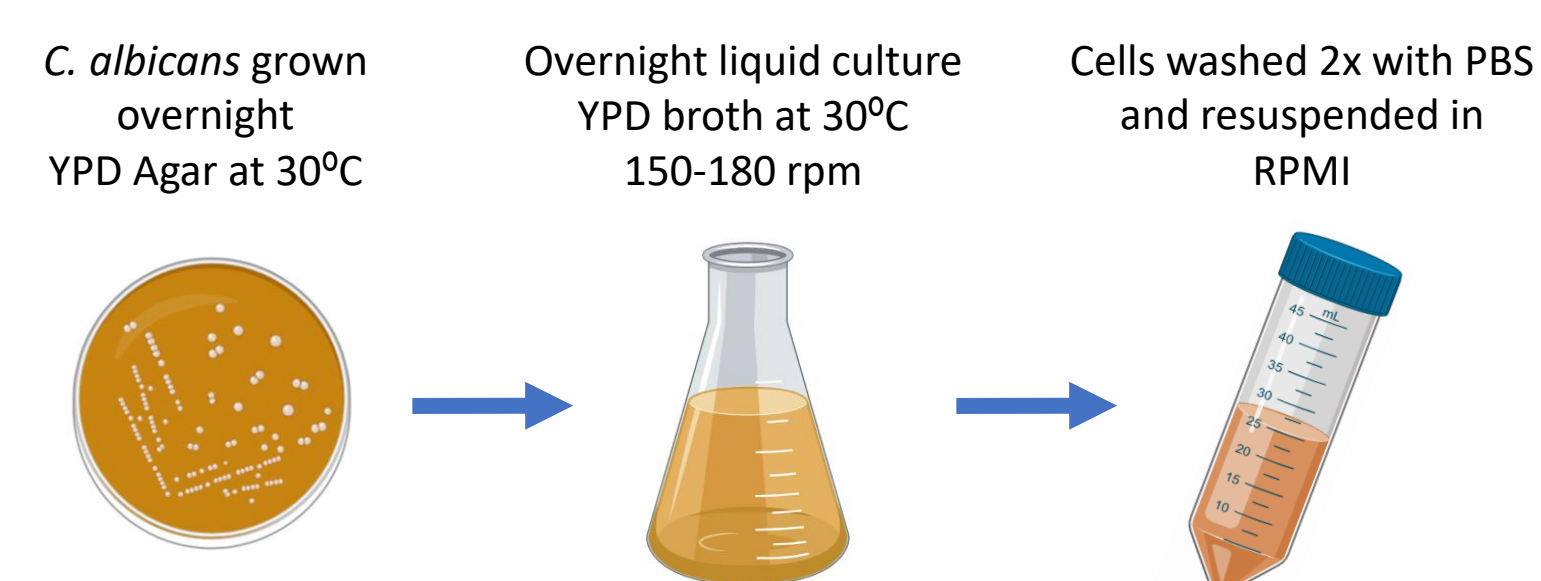
Stages of biofilm formation by *Candida albicans* over 72 hours.



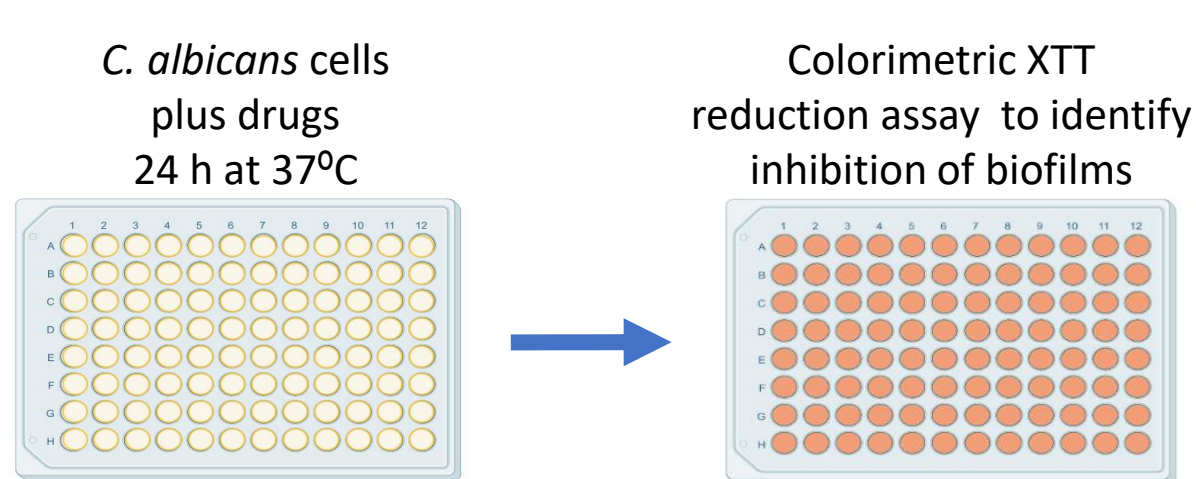
Candida albicans filamentation from yeast to hyphae.

METHODS

Preparation of *C. albicans* Cells



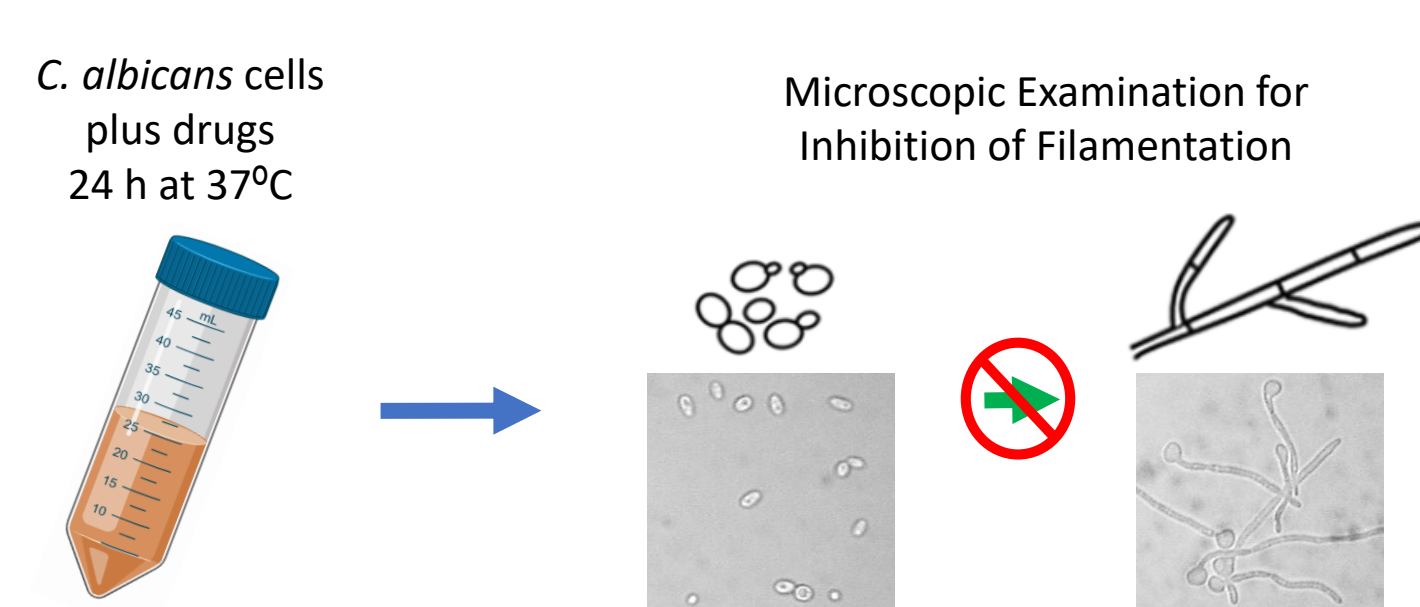
Inhibition of Biofilm Formation



Inhibition of Preformed Biofilms

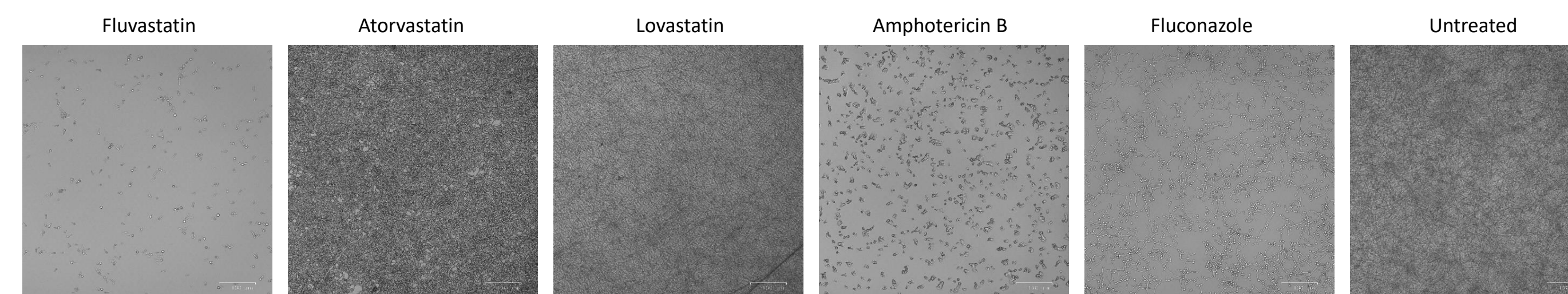
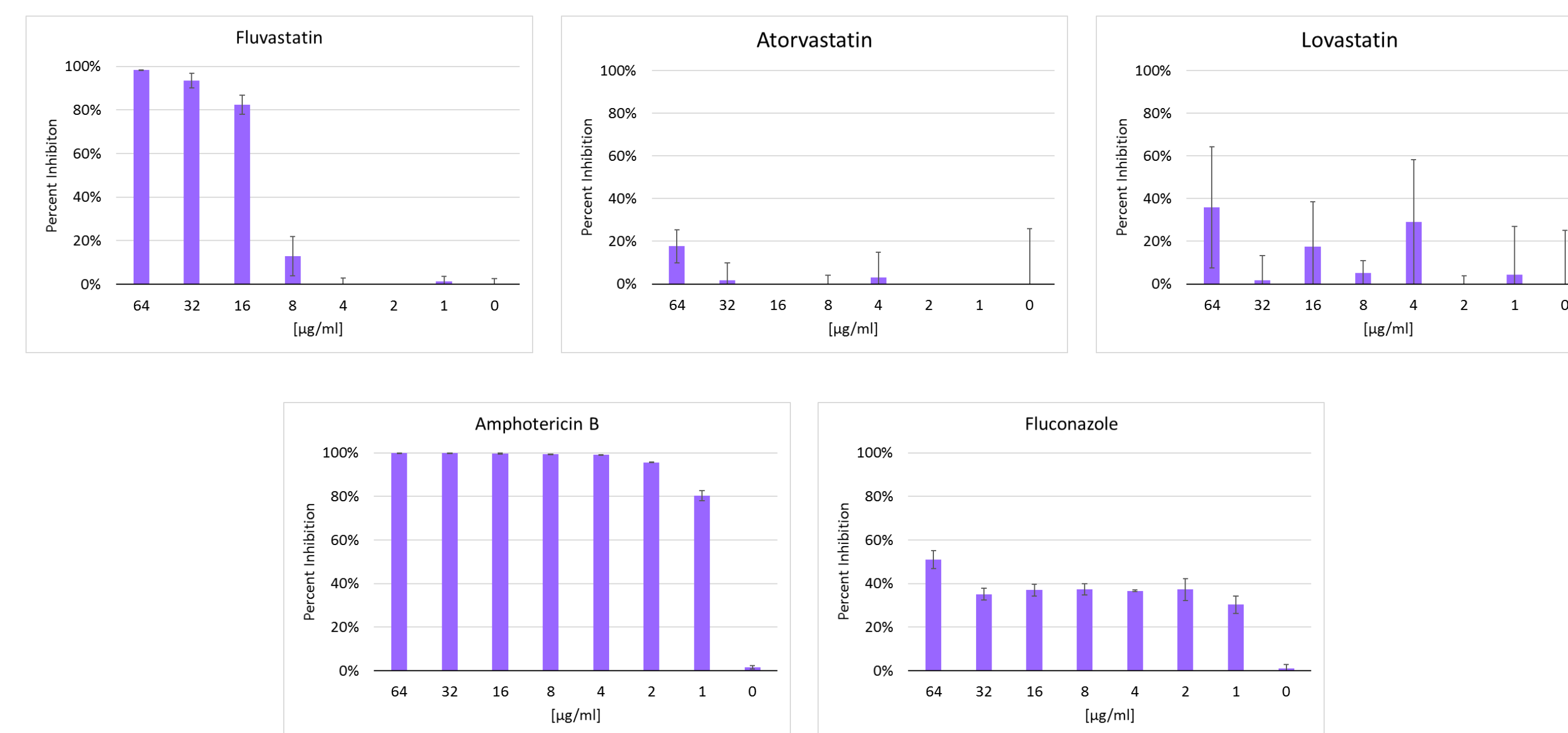


Inhibition of Filamentation



RESULTS

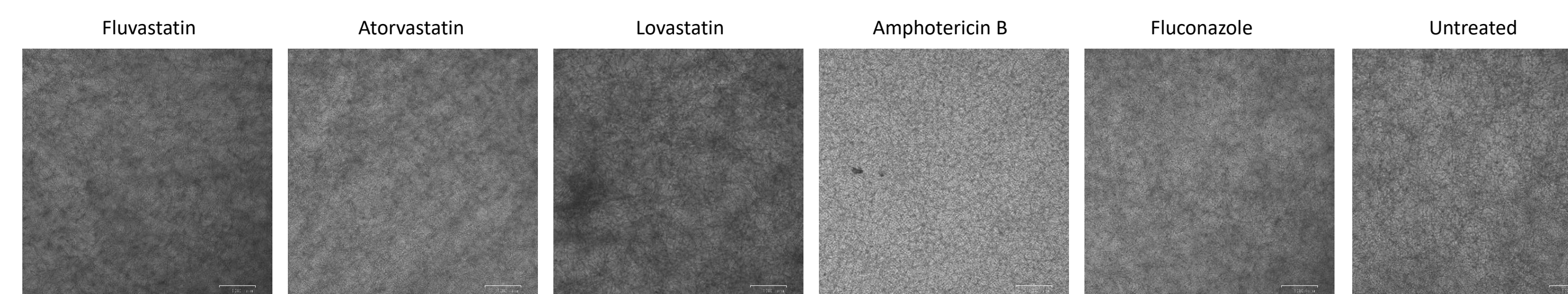
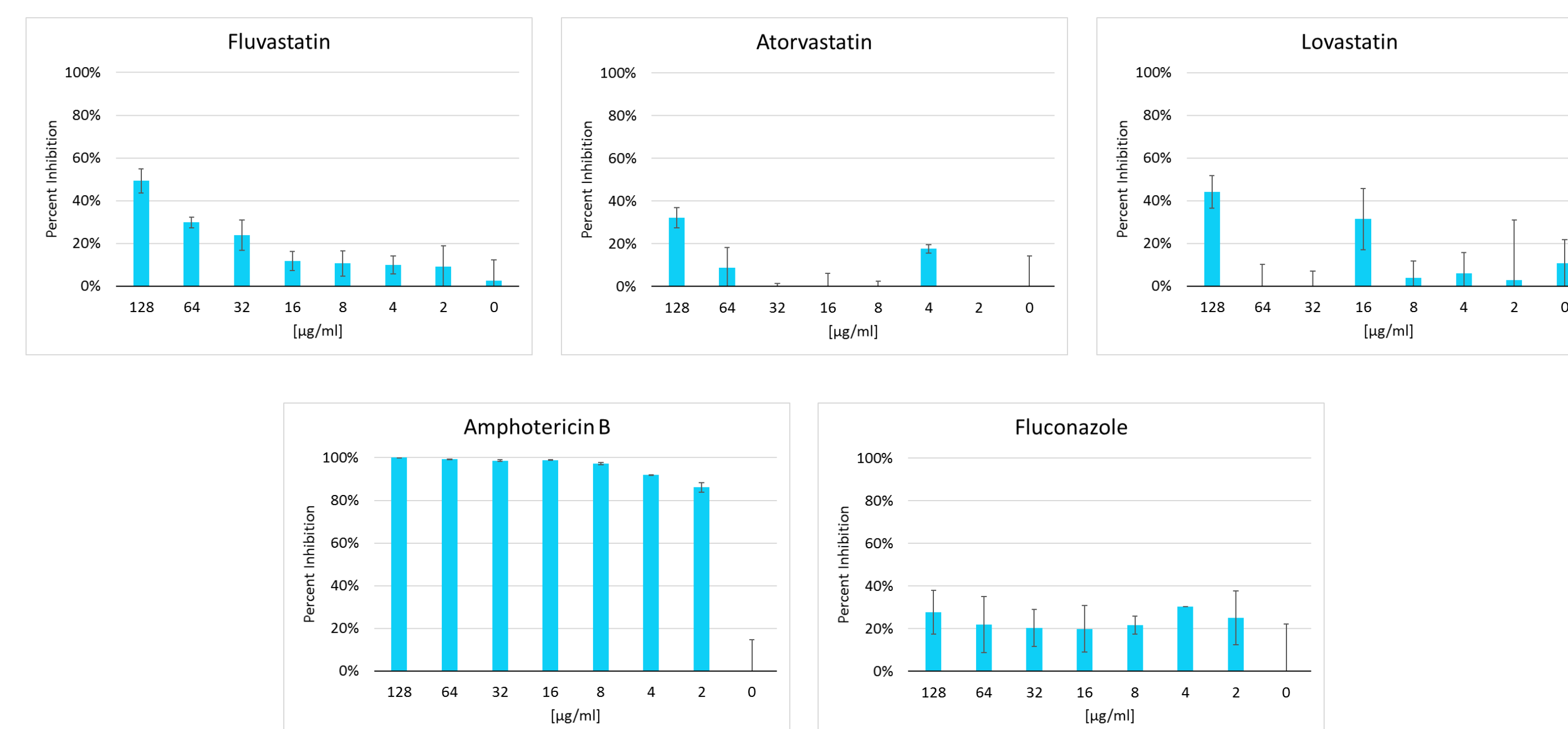
Inhibition of Biofilm Formation



Effect of statins, amphotericin B, and fluconazole on *Candida albicans* biofilm formation.

Biofilms were formed in the presence of drugs (1-64 µg/ml) for 24 hours. The graphs (top) represent the percent inhibition of biofilm formation as compared to the untreated control group (0 µg/ml). The images (bottom) are brightfield micrographs of the biofilms grown in the presence of the drugs (64 µg/ml) and without drugs (untreated). The bar represents 100 µm.

Inhibition of Preformed Biofilms

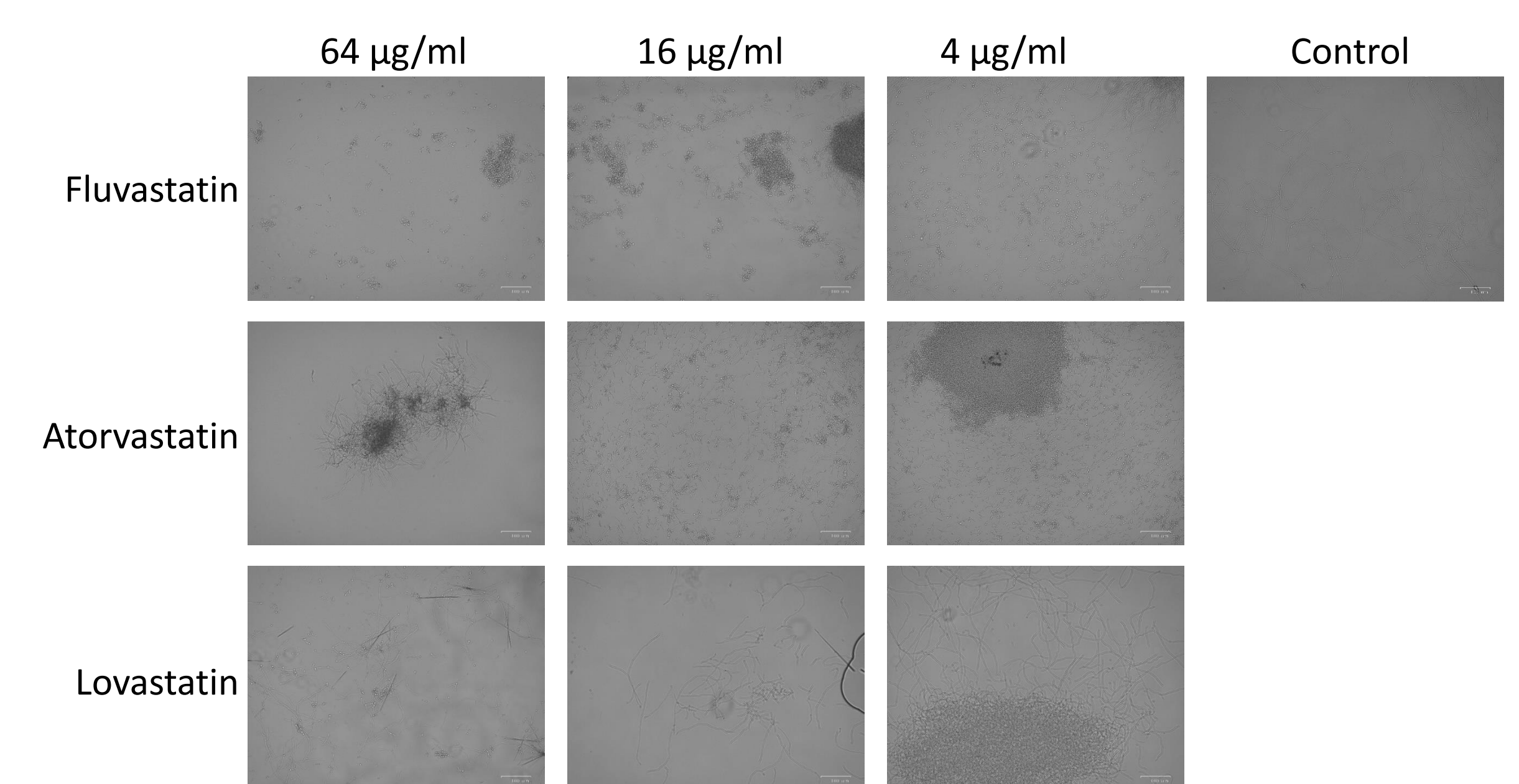


Effect of statins, amphotericin B, and fluconazole on preformed *Candida albicans* biofilms.

Biofilms were preformed for 24 hours prior to the addition of drugs (1-64 µg/ml) for an additional 24 hours. The graphs (top) represent the percent inhibition of preformed biofilms as compared to the untreated control group (0 µg/ml). The images (bottom) are brightfield micrographs of the preformed biofilms both with drugs (64 µg/ml) and without drugs (untreated). The bar represents 100 µm.

RESULTS

Inhibition of Filamentation

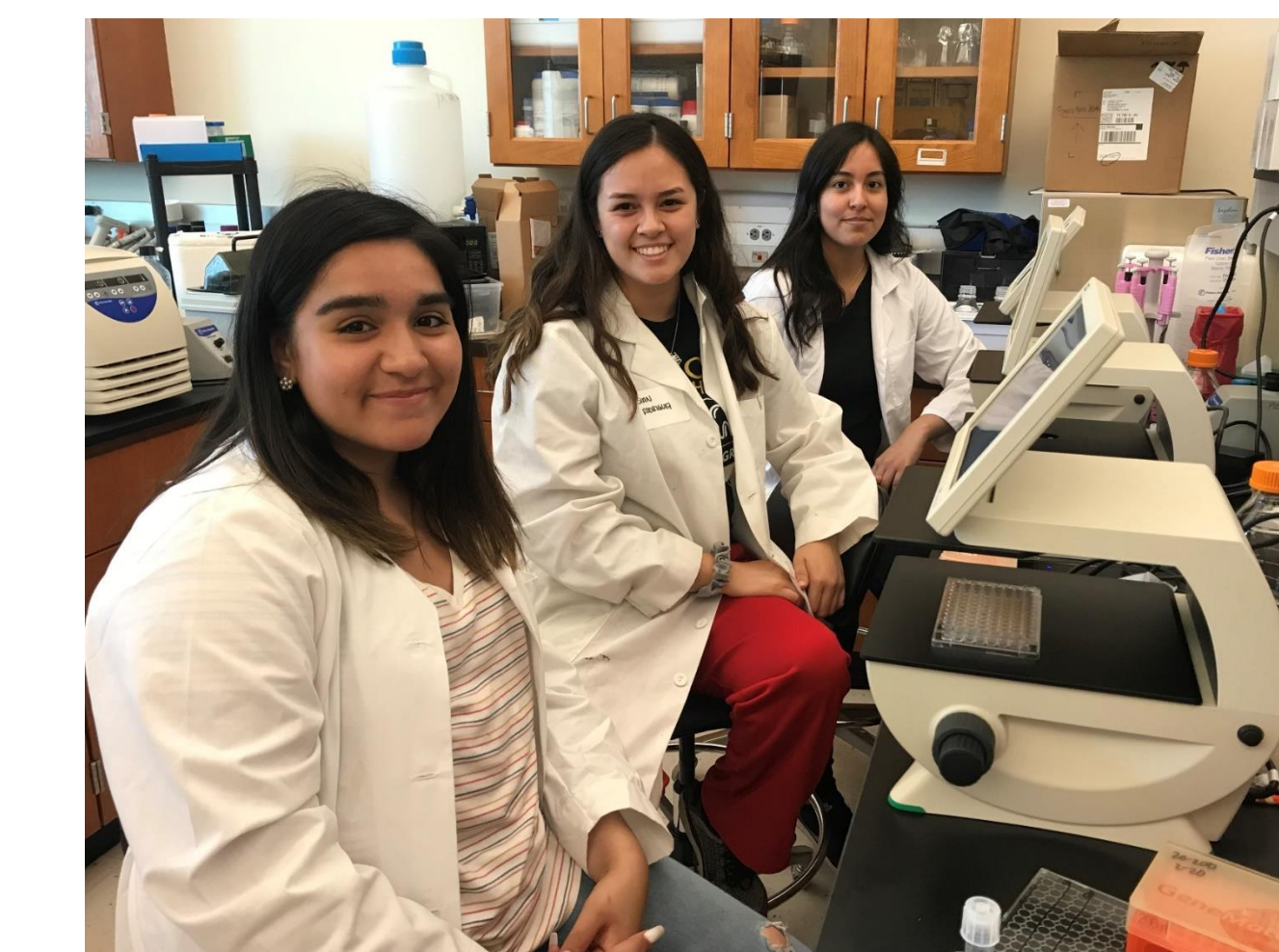


Effect of statins on *Candida albicans* filamentation.

Cells were treated with statins (64, 16, or 4 µg/ml) for 24 hours with agitation. Brightfield microscopy was used to determine the effect of the statins on filamentation (the yeast to hyphae transition). The control group is untreated. The bar represents 100 µm.

CONCLUSIONS

- Of the three statins tested, fluvastatin has the greatest activity against *Candida albicans* biofilm formation and filamentation.
- Fluvastatin inhibits *Candida* biofilm formation by more than 80% at concentrations of 16 µg/ml compared to fluconazole, a routinely used antifungal drug, which inhibits less than 50% of biofilm formation.
- Fluvastatin has reduced activity against preformed biofilms which are generally harder to treat; however, 128 µg/ml of fluvastatin inhibits approximately 50% of the preformed biofilm.
- Fluvastatin inhibits filamentation at concentrations of 4 µg/ml; whereas, the other two statins have no effect.
- Overall fluvastatin, an FDA approved medication for lowering cholesterol, could be repurposed for treating *Candida albicans* biofilm associated infections.



ACKNOWLEDGEMENTS