

**JINIS Biopharmaceuticals Co.**

## Technology Overview

### 1. Background of Technology

Polyene Macrolides is the major class of drug for fungal infection, including amphotericin B (Ambisome, Astellas; Abelcet, Enzon; Fungizone, Apoteco), nystatin (Mycostatin, Westwood Squibb), griseofluvin (Fulvicin, Schering).

Among these, amphotericin B is most commonly and conventionally used since 1960's. Amphotericin B is the mainstay antifungal agent for treatment of life-threatening mycoses and for most other mycoses, with the possible exception of the dermatophytoses. It binds to ergosterol to form ion channels and this disruption of membrane causes leakage of intracellular cations, causing cell death. Its broad spectrum of activity includes most of the medically important moulds and yeasts, including dimorphic pathogens such as *Coccidioides immitis*, *Histoplasma capsulatum*, *Blastomyces dermatitidis*, and *Paracoccidioides brasiliensis*. It is the drug of choice in treating most opportunistic mycoses caused by fungi such as *Candida* species, *Cryptococcus neoformans*, *Aspergillus* species, and the Zygomycetes.

Amphotericin B, however, must be administered intravenously and is associated with numerous side effects, ranging from phlebitis at the infusion site and chills to renal toxicity, which may be severe. Therefore, a new type of anti-fungal treatment needs to be actively sought which still has broad-spectrum antifungal activity with much-reduced side-effect, if any.

### 2. Description on Technology Applied

Figure. The isolation of marine microbes JB201 with antifungal activity

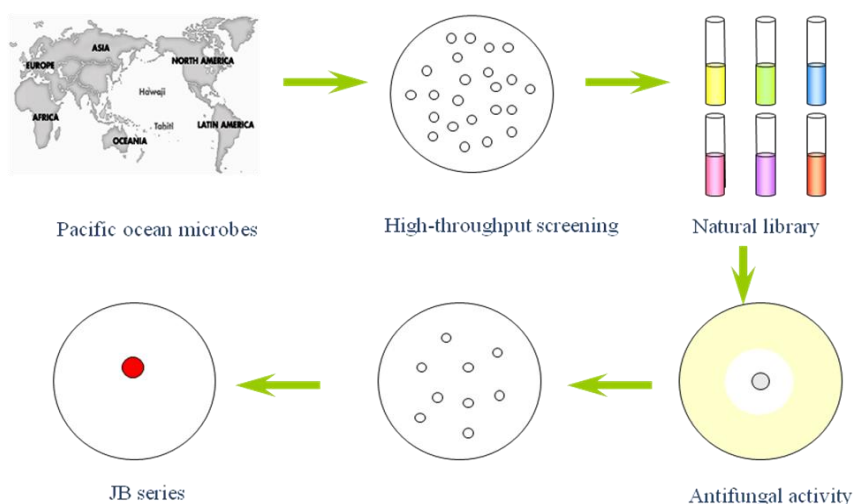


Figure. The broad-spectrum antifungal activity of JB201 to pathogenic fungi

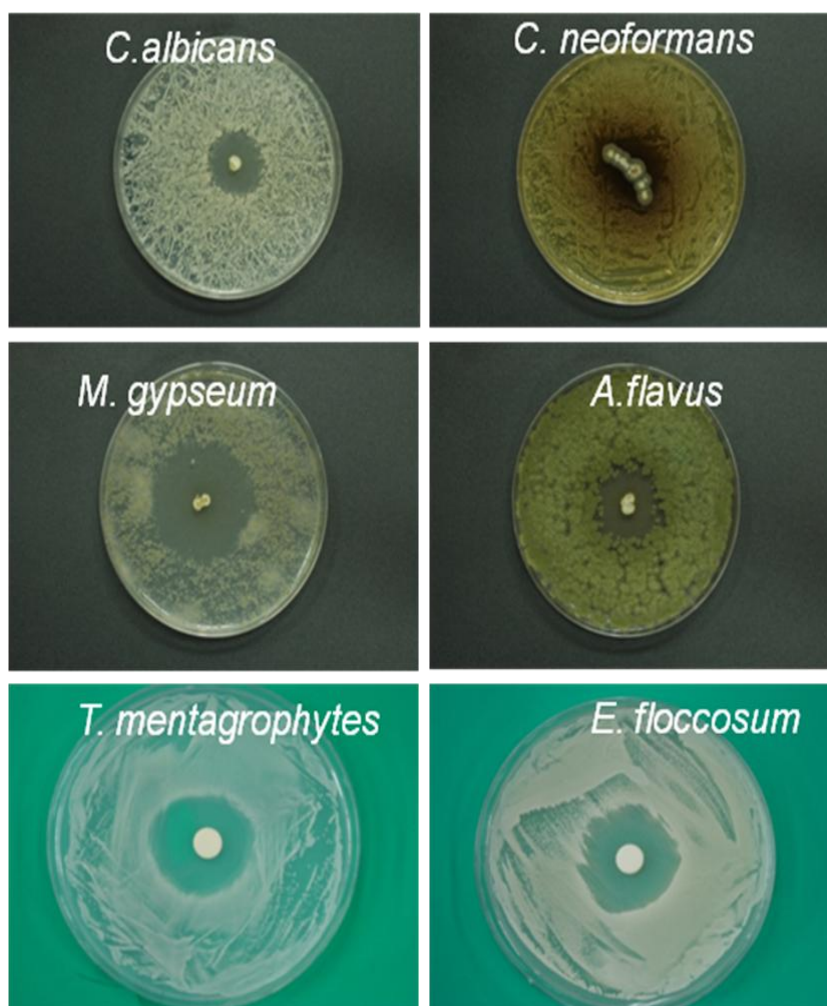
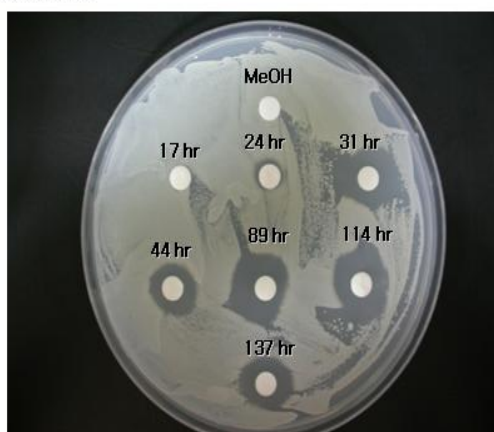


Figure. The antifungal activity of crude extract of JB201 during bioreactor culture

1. *C. albicans*



2. *C. neoformans*

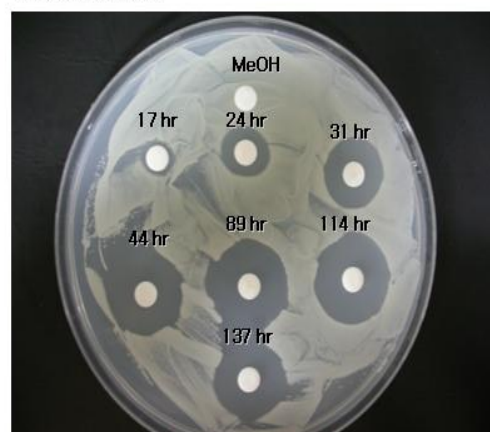
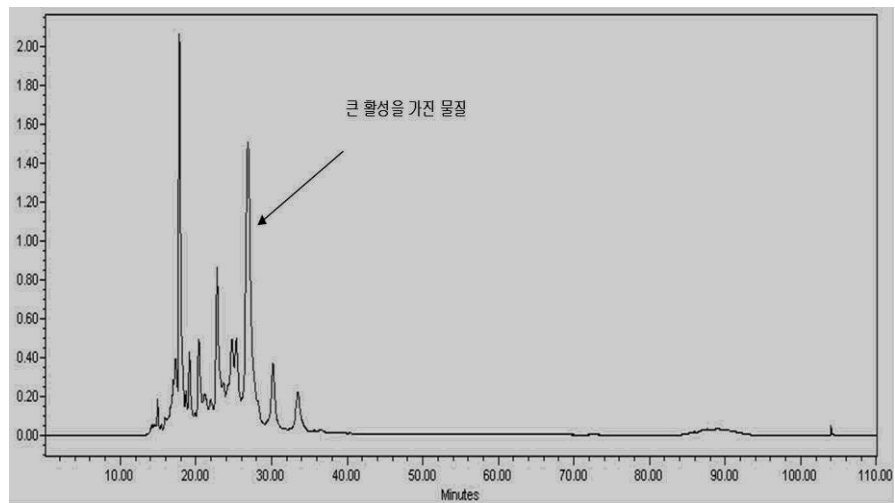
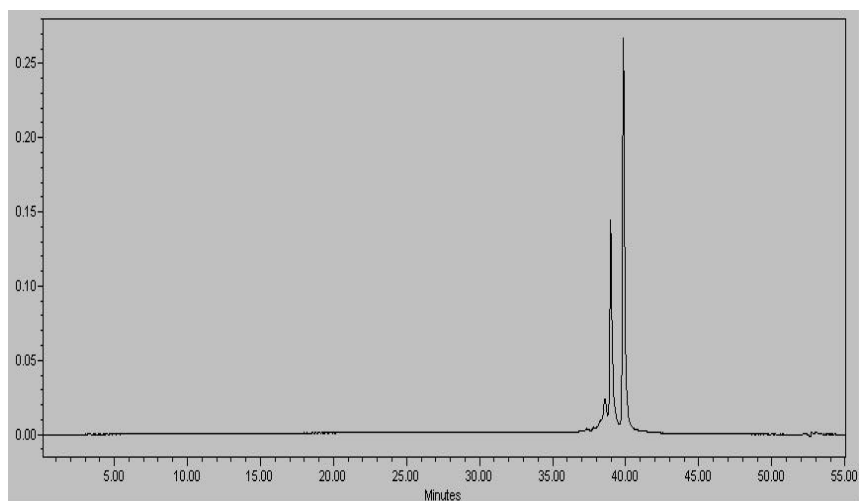


Figure. Purification of JBD201 compound from JB201 culture

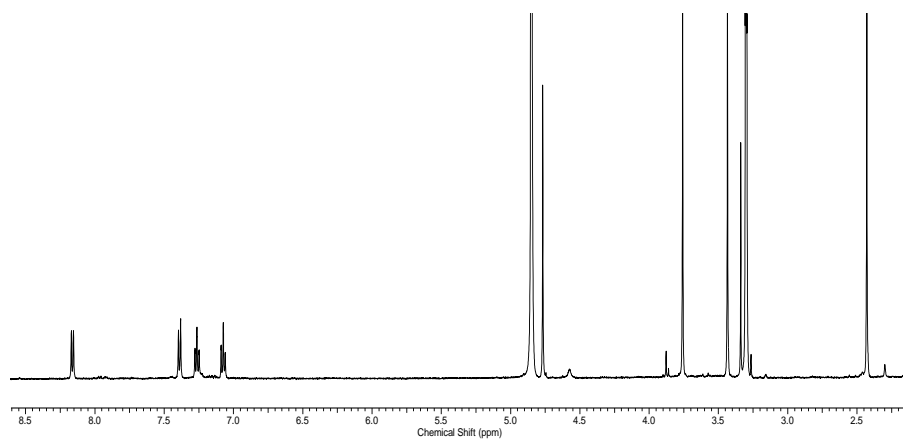


**Semi-prep HPLC chromatogram**



**Analytical HPLC chromatogram**

Figure. Structure analysis of JBD201 compound by NMR



JINIS JBD-201, as summarized below, is a novel polyene compound which binds ergosterol, disrupting the fungal membranes.

- Class: Belongs to Polyene macrolide family
- Novel compound with unknown structure: Patent in preparation
- Mode of action: Binds to ergosterol and disturb fungal membrane
- Origin: Isolated from marine derived microorganism, *Streptomyces JB201*
- Spectrum: Broad spectrum antifungal and active against most molds
- Acute toxicity: less than Amphotericin B

### **3. Differential Point, Superiority or Characteristics of Technology Applied**

The world market for antifungal agents is currently in excess of US\$5 billion with an annual double-digit growth, expected to 7 billion by 2011 (Kalorama Information). This market for systemic agents for serious infection is currently served by only three major drug classes, azoles, polyenes and echinocandins.

Given that patient numbers are increasing, primarily due to impaired immune status, and that crude mortality from invasive aspergillosis is around 85% and for Candida bloodstream infections is 40%, new drugs with broad-spectrum efficacy and less toxicity are required.

JBD-201 could be developed as NEW broad-spectrum antifungal therapeutic for treatment of systemic fungi infections such as candidiasis, aspergillosis and cryptococcal meningitis as well as opportunistic fungal infection.

## Specific Patent

| No. | Name of Patent           | Application No. | Date of application | Country | Status (Applied/approval) | Cost for patent (KRW) |
|-----|--------------------------|-----------------|---------------------|---------|---------------------------|-----------------------|
|     | New antifungal compounds |                 | 2009.               | Korea   | (In preparation)          |                       |
|     |                          |                 |                     |         |                           |                       |

※ Please provide accurate information for Application No and Date of application/approval. It will be used for patent search.

※ In case of Cost for patent, please consider administrative cost for patent application only.

※ In case of PCT or overseas patent (application) except domestic patent, Please attach a certificate of application/approval (or patent abstract) as a separate file.