Latrunculins A and B

Storage upon receipt:
- \( \leq -20^\circ\text{C} \)
- Desiccate

Absorption:
- \( 215 \pm 3 \text{ nm (latrunculin A in methanol)} \)
- \( 212 \pm 3 \text{ nm (latrunculin B in methanol)} \)

**Introduction**

Latrunculins A and B are cell-permeant macrolides containing the rare 2-thiazolidinone ring. Latrunculin A has a 16-member ring, and latrunculin B a 14-member ring (Figure 1). These marine toxins are derived from sponges and nudibranchs, most notably the Red Sea sponge *Negombata magnifica*, formerly *Latrunculia magnifica*. Latrunculins disrupt microfilament polymerization due to a one-to-one binding with monomeric G-actin but have no effect on microtubular structure. Latrunculin A inhibits binding of thymosin \( \beta_4 \) and nucleotide exchange on actin, but does not inhibit binding by profilin or DNase I. Latrunculin A is more potent than latrunculin B, with both showing 10- to 100-fold greater potency than cytochalasins.

**Contents**

Latrunculins are provided as a lyophilized powder that is stable for 2 to 3 years when stored at \( \leq -20^\circ\text{C} \) and desiccated. They should be reconstituted in either anhydrous DMSO or ethanol (100 mg/mL for latrunculin A; 25 mg/mL for latrunculin B), stored at \( \leq -20^\circ\text{C} \), desiccated, and protected from light. Stock solutions are stable for at least 2 to 3 months at \( \leq -20^\circ\text{C} \), with latrunculin A exhibiting slightly better stability than latrunculin B. Latrunculin B should not be used in the presence of serum containing media. Both are sensitive to acids and bases, however latrunculin A is the more labile of the two in the presence of these agents.

**Notes**

The experiments described below are summarized from various peer-reviewed scientific journal articles. See *References* for specific citations.

**Cell-Based Assays**

Latrunculin A has a \( K_d \) of 180 nM–220 nM (as determined by measuring changes in fluorescence intensity with pyrene-labeled purified rabbit skeletal muscle actin in 5 mM Tris pH 7.8 containing 0.1 mM CaCl\(_2\), 2 mM MgCl\(_2\), 0.2 mM ATP, 0.2 mM DTT, 0.1% sodium azide at 25°C); latrunculin B has a \( K_d \) of ~200 nM. Latrunculin treatment caused complete rounding up of cells (mouse neuroblastoma and hamster fibroblasts) at 0.1–0.2 \( \mu \text{g/mL} \) (latrunculin A) and 0.5 \( \mu \text{g/mL} \) (latrunculin B) after 1 hour incubation. At 0.04–0.05 \( \mu \text{g/mL} \) of latrunculin A, most cells retained their normal shape, but some cells contracted and adopted aberrant morphologies. Cells treated with latrunculin A maintained their altered state for extended periods (up to one week following treatment). Latrunculin B–induced changes appear to be more transient (effective anywhere from a few minutes to a few hours), even when cells were continually incubated with the compound. (The authors of the study suggested that latrunculin B may have been inactivated by the serum in the growth media).

**Solution Assays with Purified Actin**

Stock solutions of latrunculins were made to 2 to 10 mM in DMSO and diluted to 100 \( \mu \text{M} \) in Buffer G (Buffer G: 5 mM Tris, pH 7.8, 2 mM MgCl\(_2\), 0.1 mM CaCl\(_2\), 0.2 mM ATP, 0.2 mM DTT, 0.01% to 0.1% sodium azide). Increases in fluorescence signal upon polymerization were monitored at room temperature using pyrenyl-actin (actin labeled on Cys374 with \( N-(1-\text{pyrene})\text{iodoacetamide} \) (Molecular Probes, Catalog number P29)), using 0.7–0.95 moles of label per mole of protein according to the method of Koyama and Mihashi.
References


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<tr>
<td>L22290</td>
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Invitrogen European Headquarters
Invitrogen, Ltd.
3 Fountain Drive
Inchinnan Business Park
Paisley PA4 9RF, UK
Phone: +44 (0) 141 814 6100 • Fax: +44 (0) 141 814 6260
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