Effects of Amphotericin B on Renal Transport

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Dear Sir,

Amphotericin B is an effective antifungal agent, the clinical use of which is limited by its renal toxicity. Both its antifungal and nephrotoxic effects have been ascribed to strong membrane affinity and subsequent alteration of cell membrane activity, particularly ion permeability. This report describes alterations in membrane function induced by amphotericin B in purified renal tubule membranes.

Rabbit renal membranes were purified through a series of centrifugation and homogenation steps. The activity of membrane transport was observed using the potential sensitive dye 3,3'-dipropylthiadicarbocyanine iodide [1]. Because Na⁺-dependent transport systems are electrogenic, their activity can be observed as changes in membrane potential, which, in turn, are proportional to the observed fluorescence response of the dye [2].

In the absence of amphotericin B, the kinetics of Na⁺-dependent transport was observed and demonstrated classical saturable response (fig. 1, top curve). In the presence of 2.0 µg/ml amphotericin B, the rate of transport was decreased significantly (fig. 1, lower curve). The specificity of these measurements for Na⁺-dependent transport were confirmed by the observation that in the absence of Na⁺, there was no observable membrane potential change at any concentrations of transportable metabolite (fig. 1, baseline).

The four metabolites phenylalanine, glucose, prolene and alanine demonstrated inhibition by 45, 60, 50 and 45%, respectively. Because amphotericin B significantly alters renal membrane permeability, it is believed that the apparent inhibition of transport may be the result of altered membrane permeability, particularly Na⁺. These observations suggest that amphotericin B can induce changes in purified renal membranes which profoundly alter membrane transport in addition to its direct effects on ion permeability.

0 2 4 6 8 10
[Phenylalanine], mM

Fig. 1. Kinetics of Na⁺ dependent transport of phenylalanine.

References

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