

Título: ANALYTICAL APPROACH TO IN VITRO STUDIES OF THE ECHINOCANDIN
CASPOFUNGIN/KASPOFUNGINA EKINOKANDINAREN IN VITRO AZTERLANEN IKUSPEGI ANALITIKOA. //
ANALYTICAL APPROACH TO IN VITRO STUDIES OF THE ECHINOCANDIN
CASPOFUNGIN/KASPOFUNGINA EKINOKANDINAREN IN VITRO AZTERLANEN IKUSPEGI ANALITIKOA.

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Resumen: It is known that invasive fungal infections have become a concern around the world due to the morbidity and mortality shown. The main responsible of these infections are aspergillus, cryptococcus and candida genus. However, candida has gained the attention of specialists due to the mortality shown in some population groups, where it can arrived to 40 %. Invasive candidiasis is treated with four antifungal drug families: azoles, polyenes, pirimidine analogues and echinocandins. Because of their use, fungi have developed different resistance mechanisms to ensure their proliferation even in presence of the drugs. As resistance mechanisms to echinocandin family remain, low specialists use them as a first-line therapy for invasive candidiasis.

Unfortunately, in the last decade resistance of *C. glabrata* species to echinocandins has risen, especially to caspofungin (CSF). In this context, this work presents a deep sight of how to work with CSF in in vitro studies. First, an analytical methodology for the quantification of CSF in RPMI-1640 cell culture media has been developed and validated successfully. Secondly, the attempt of studying *C. glabrata*'s resistance to CSF has been done, by means of two compartment pharmacokinetic/pharmacodynamic in vitro model. Finally, a stability study of CSF has been carried out checking degradation and adsorption possibilities. Results obtained shown the difficulties of working with CSF in human body conditions (pH around 7 and in aqueous solution) due to the adsorption phenomenon. This research provides a new perspective to assess the results obtained previously in microbiological and therapeutic fields and, supports researchers to go deeper in the evaluation of the reliability of the methodologies used for resistance determination and drug administration. // It is known that invasive fungal infections have become a concern around the world due to the morbidity and mortality shown. The main responsible of these infections are aspergillus, cryptococcus and candida genus. However, candida has gained the attention of specialists due to the mortality shown in some population groups, where it can arrived to 40 %. Invasive candidiasis is treated with four antifungal drug families: azoles, polyenes, pyrimidine analogues and echinocandins. Because of their use, fungi have developed different resistance mechanisms to ensure their proliferation even in presence of the drugs. As resistance mechanisms to echinocandin family remain, low specialists use them as a first-line therapy for invasive candidiasis. Unfortunately, in the last decade resistance of *C. glabrata* species to echinocandins has risen, especially to caspofungin (CSF). In this context, this work presents a deep sight of how to work with CSF in in vitro studies. First, an analytical methodology for the quantification of CSF in RPMI-1640 cell culture media has been developed and validated successfully. Secondly, the attempt of studying *C. glabrata*'s resistance to CSF has been done, by means of two compartment pharmacokinetic/pharmacodynamic in vitro model. Finally, a stability study of CSF has been carried out checking degradation and adsorption possibilities. Results obtained shown the difficulties of working with CSF in human body conditions (pH around 7 and in aqueous solution) due to the adsorption phenomenon. This research provides a new perspective to assess the results obtained previously in microbiological and therapeutic fields and, supports researchers to go deeper in the evaluation of the reliability of the methodologies used for resistance determination and drug administration.