

アンジオテンシン II 変換酵素阻害薬
オルメサルタンメドキシミルのヒト血清アルブミンによる
加水分解及びその触媒部位の同定

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**Hydrolysis of angiotensin II receptor blocker prodrug olmesartan
medoxomil by human serum albumin and
identification of its catalytic active sites.**

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ABSTRACT : In the present study, we investigated the esterase-like activity of human serum albumin (HSA) and the mechanism by which it hydrolyzes, and thereby activates, olmesartan medoxomil (CS-866), a novel angiotensin II receptor antagonist. We found that the hydrolysis of CS-866 by HSA followed Michaelis-Menten kinetics. These findings suggest that the hydrolytic activity is associated to parts of site I and site II for ligand binding. All the mutant HSAs tested exhibited a significant decrease in reactivity, suggesting that Lys-199, Trp-214, and Tyr-411 play important roles in the hydrolysis. Results obtained using a computer docking model are in agreement with the experimental results.

抄録 今回、我々はヒト血清アルブミン (HSA) の esterase 活性によりオルメサルタンメドキシミルが加水分解されることまた、その触媒部位としてLys-199、Trp-214、Tyr-411が重要であることを変異体及びドッキングモデルにより明らかにした。

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