PARALLEL QM/MM X-RAY REFINEMENT OF PROTEIN BOUND ANTI-ALZHEIMER DRUG DONEPEZIL

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Donepezil is a piperidine-based potent anti-Alzheimer drug designed to reversibly inhibited acetylcholinesterase. In this study the conformational profiles of bound donepezil have been determined using parallel QM/MM X-ray refinement approach based on our upgraded in-house *ab initio* code QUICK, which currently can support MPI (Message Passing Interface) with linear scaling divide and conquer algorithm in an effort to accelerate calculation by parallel. In the re-refined donepezil conformer, coordinate errors existed in the PDB deposited geometry were significantly fixed thereby enhancing the interaction between donepezil and several aromatic residues (e.g. Trp84, Trp279 and Phe330) intensively. As a result there was a 93% reduction in donepezil conformation strain using the QM/MM refined structure versus the original PDB donepezil conformation. Hence our parallel QM/MM X-ray refinement protocol can offer reliable anti-Alzheimer drug-receptor structural information for use in innovatively designing more effective anti-Alzheimer drugs.