Infections caused by microorganisms are an enormous problem to human health. Thus, the resistance development by such microorganisms becomes a remarkable challenge, disabling conventional antibiotics or requiring the ingestion of higher doses of them. Antimicrobial peptides (AMPs) have been proposed as an alternative of infectious diseases treatment, due their activity against a wide range of pathogens. Among them are the defensins, which are cysteine-rich AMPs commonly found in animals, plants and fungi. They could be an alternative for developing antimicrobial agents through rational design techniques. In this work physico-chemical and structural characteristics of HBD1 (Human Beta Defensin 1) were analyzed to develop analogues by rational design.

Here structural analysis of the HBD1’s dimerization and further analysis of their amino acid conservation in orthologs were used for developing the pattern DXYCXSXGGQCXYSCPX(6)GTCYRGKAKCCX. This pattern was used as a constraint for the genetic algorithm, which used CS-AMPPred as the fitness function. The physicochemical properties evolution during the simulations was computed. The best sequences from the 10 highest fitness simulations were selected.

The pattern developed demonstrated that the C-terminal region \( ^{25}GTCYRGKAKCC^{35} \) is extremely conserved. Physicochemical properties analyses along the algorithm iterations shows that there is an increase on peptide net charge, as well as, an increase in propensity for loop formation and flexibility. Only one out of ten sequences showed the highest fitness values was incapable to form dimer, unlike the native structure. This sequence presented an arginine at position 8, near dimerization site, which seems to generate electrostatic repulsion, destabilizing the dimer.

The data generated shed some light over the HBD1 dimerization process. Furthermore, the sequences generated demonstrated the importance of arrangement of charged residues near dimerization site might influence the peptide dimerization. In summary, data here presented present HBD1 as a new target to drugs development and rational design techniques.

**Keywords:** Genetic Algorithm; Antimicrobial peptides; Rational design; Defensins.

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