The study of the correlation of the binding energy of peptide ligand complexes with hybrid antibiotics vancomycin-azithromycin and eremomycin-azithromycin with antibacterial activity

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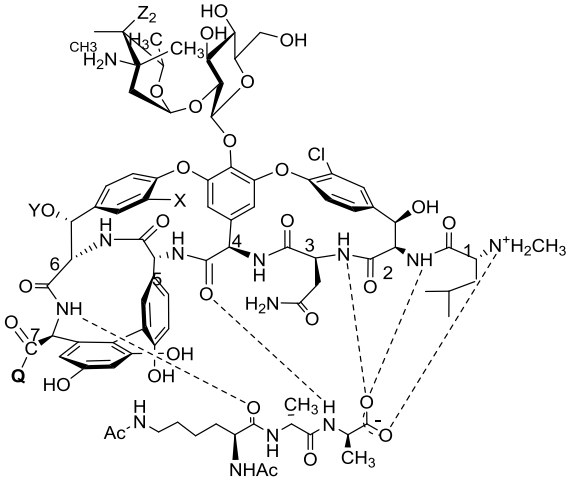
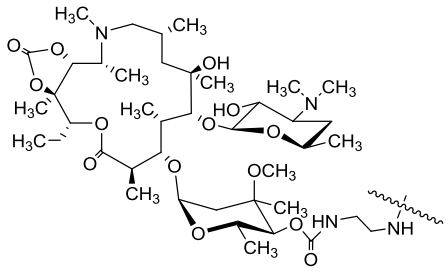
One of modern strategies that can solve the problem of antibacterial resistance is the development of dual-acting hybrid antibiotics – structures that contain two covalently linked antimicrobial drugs that interact with different targets in a bacterial cell [1].
Antibacterial activity of hybrid antibiotics vancomycin-azithromycin (C11, C12-carbonate) and eremomycin-azithromycin (C11, C12-carbonate) was evaluated. Quantum chemical calculations of energy these hybrid antibiotics with a model tripeptide ligand α,ε-di-Ac-*L*-Lys-*D* -Ala-*D*-Ala by the semiempirical PM6 method using a software package Spartan·10[2] provided data on geometrical parameters of these complexes along with the energy of their formation and the influence of protonation of the $NHCH_3$ group. A correlation between the energy of formation of antibiotics-ligand complexes and antibacterial activity of hybrid antibiotics against Gram-positive bacterial strains was found



A) α, ε - di-Ac-L-Lys-D -Ala-D-Ala (**LAA-**)



Vancomicin$^+$ + LAA- (1a)

R=OH; X=Cl; Y=H;
Y=эремозаминил–α
Z_1=OH; Z_2=H; **Q**=OH

Eremomycin$^+$ + LAA- (2a)

R=OH; X=H;

Z_1=H; Z_2=OH; **Q**=OH

Vanco-azithro$^+$ + LAA- (5a) Q =

Eremo-azithro$^+$ + LAA- (6a) Q=

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References

[1] A N Tevyashova, E N Olsufyeva, M N Preobrazhenskaya, "Design of dual action antibiotics as an approach to search for new promising drugs", *RUSS CHEM REV*, 2015, **84** (1), 61–97

[2] https://www.wavefun.com/