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Determining Favorable Binding Configurations of the Anti-Cancer Drug Ellipticine to the KV11.1 Potassium Channel V-VI Transmembrane Domain Through Autodock Simulations DAWN LIPSCOMB, University of Texas at San Antonio, SAVERIO GENTILE, Loyola University Chicago, LORENZO BRANCALEON, University of Texas at San Antonio — Ellipticines such as 9-methoxy-N-2-methylellipticinium acetate (MMEA) and 9-hydroxy-N-2-methylellipticinium acetate (NMEA, Celiptium ®) are antineoplastic drugs that exert their selective cytotoxicity against leukemia and endometrial carcinoma. Ellipticine's action is also related to severe physical side effects, but the link between undesired effects and pharmacological application is not well understood. We investigated the binding of Ellipticine derivatives with the Kv11.1 potassium ion channel using Autodock and revealed that hydroxyellipticinium derivatives provide binding configurations with Kv11.1, but the energy, location and estimated dissociation constant varied. The binding energy is as follows: Chloroceliptium (-6.60 kcal/mol) > Celiptium (- 6.37 kcal/mol) > Methoxyceliptium (- 6.20 kcal/mol) > Datelliptium (-6.08 kcal/mol). Autodock simulations demonstrate that binding affinity is high at opposing ends of the channel and low within the channel interior. These favorable binding configurations suggest that Ellipticine derivatives may bridge among end subunits of the channel and potentially inhibit the flow of ions.

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