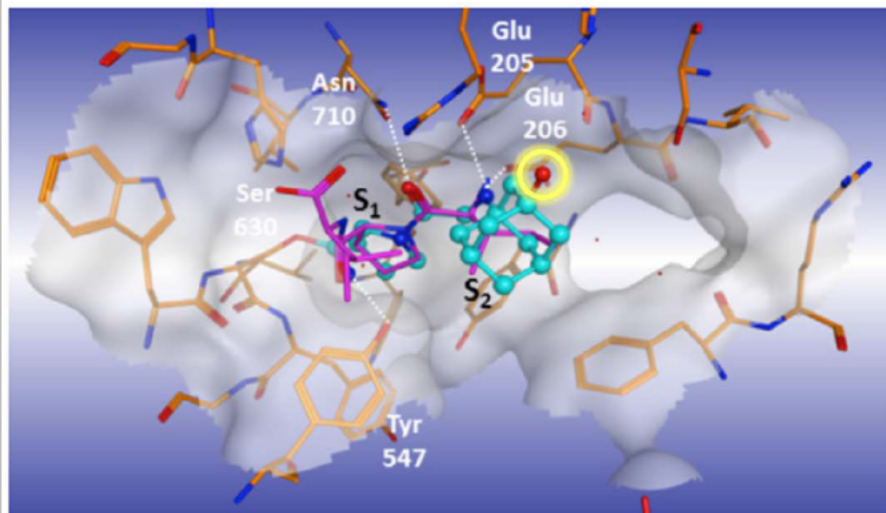


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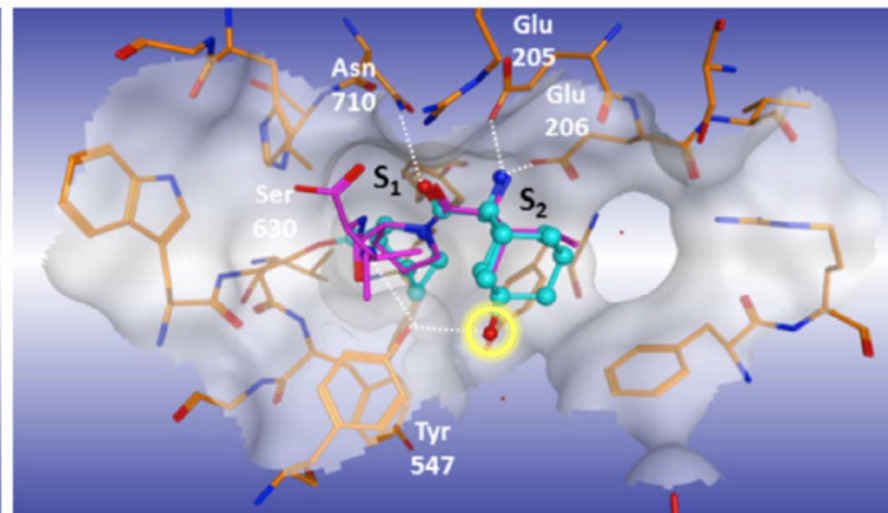
Binding Interactions of Vildagliptin and Saxagliptin

Vildagliptin



The hydroxyl group on the adamantyl moiety forms hydrogen bonds with His126 and Ser209 via the water molecules.

Saxagliptin



Although it was originally intended to enhance the chemical stability of the cyanopyrrolidine [3], introduction of the cyclopropane moiety afforded an additional hydrophobic interaction with the side chain of Tyr666 in the S₁ subsite. Moreover, the direct hydrogen bond between the hydroxyl group of saxagliptin and the side chain of Tyr547 may also contribute to its higher potency.

Ex. 2176 at 3 and 4