

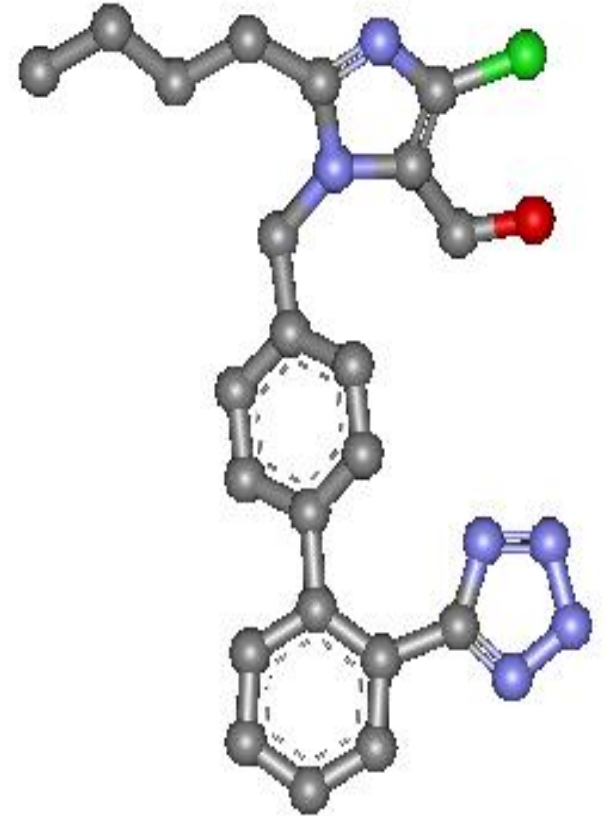
Bilgisayar Destekli İlaç Tasarımının Tarihçesi ve Gelişmesi

- **60 – 70 ler ... QSAR**
- **80 ler ... Moleküler Modelleme**
- **90 ların başı ... 3D (3 Boyutlu) Tarama, Hedef Tabanlı İlaç Tasarımı (de Novo tasarımı)**
- **90 ların sonu ... Kombinatoriyal Kimya, HTS (High Througput Screening)**
- **00 ler ... Tüm Yöntemlerin birarada kullanımı**

QSAR +Moleküler Modelleme

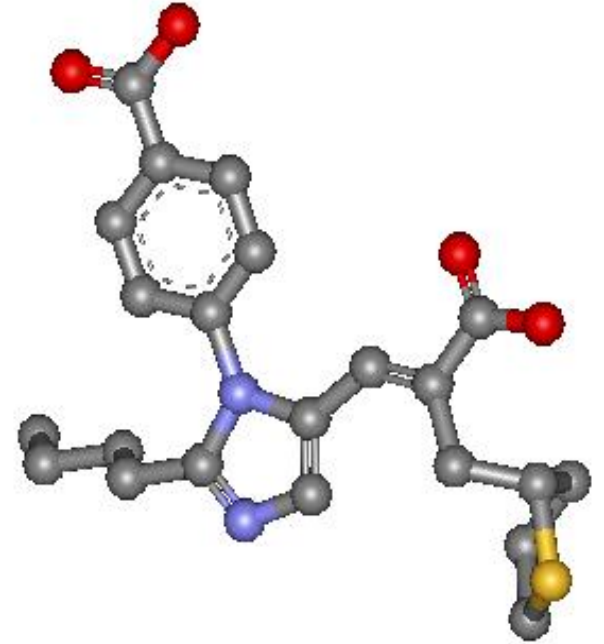
Çalışmaları Ürünü

- COZAAR® for Antihipertansif - DuPont, Merck
- Losartan: Angiotensin II reseptör antagonisti
- Duncia, J. V. *et al. J. Med. Chem.* **1990**, 33, 1312-1329; Duncia, J. V. *et al. Med. Res. Rev.* **1992**, 12, 149-191.



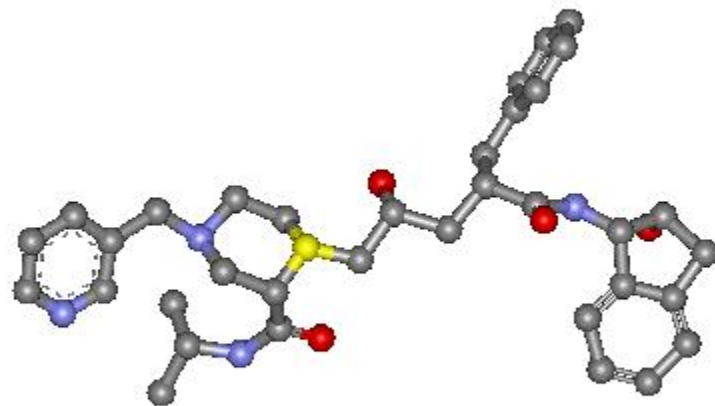
Moleküler Modelleme ürünü

- TEVETEN® Hipertansiyon Tedavisinde kullanılır - Smithkline Beecham
- Eprosartan: Angiotensin II receptör antagonisti
- Weinstock, J. *et al. J. Med. Chem.* **1991**, 34, 1514-1517;
Keenan, R. M. *J. Med. Chem.* **1993**, 36, 1880-1892.



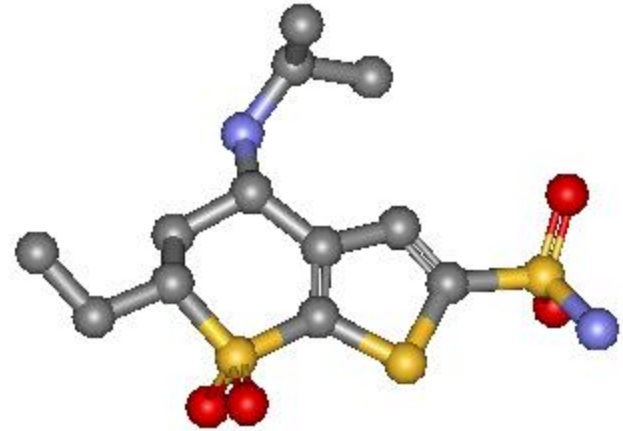
Hedef Tabanlı Tasarım (SBD)

- CRIVAN® for AIDS – Merck
- Indinavir: HIV-1 Protease Inhibitor developed via X-ray crystallography, molecular mechanics calculations, and structure-based design
- Dorsey, B. D. *et al.* *J. Med. Chem.* **1994**, 37, 3443-3451; Holloway, M. K. *et al.* In *Computer-Aided Molecular Design*, Reynolds, C. H. *et al.*, Eds. ACS Symp. Series 589, 1995, 201-210
- Merck researchers involved with this study have received ACS Award for "Outstanding Achievement in Molecular Design"



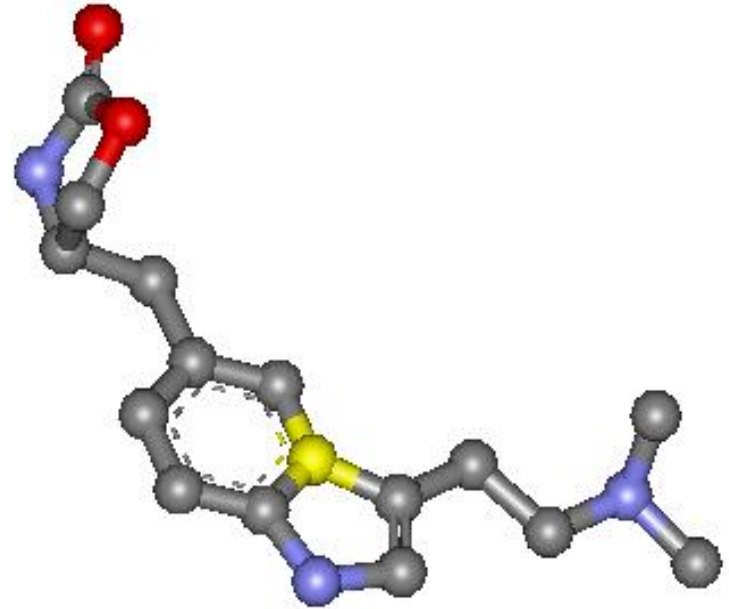
Hedef Tabanlı Tasarım ve *ab initio* hesaplamaları Ürünü

- TRUSOPT® for Glokom Tedavisinde - Merck
- Dorzolamide: Karbonik Anhidraz İnhibitörü
- Greer, J. *et al.* *J. Med. Chem.* **1994**, 37, 1035-1054; *J. Med. Chem.* **1989**, 32, 2510

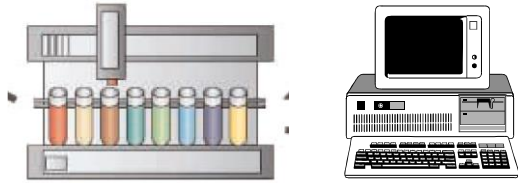


Farmakofor Analizleri (Moleküler Modelleme) Ürünü

- ZOMIG® Migren tedavisinde - Wellcome, Zeneca
- Zolmitriptan: 5HT₁-agonisti
- Glen, R. C. *et al. J. Med. Chem.* **1995**, 38, 3566-3580.



TGF- β Inhibitörü

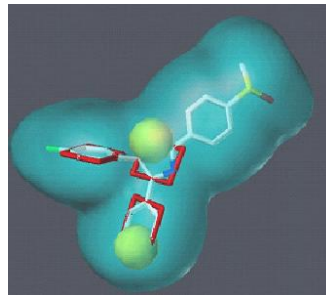
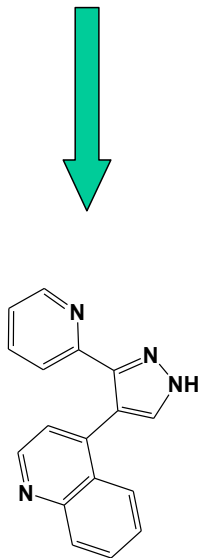


200,000
compounds

HTS Yöntemi

Eli Lilly

↓
Drug Target (eg. T β RI)



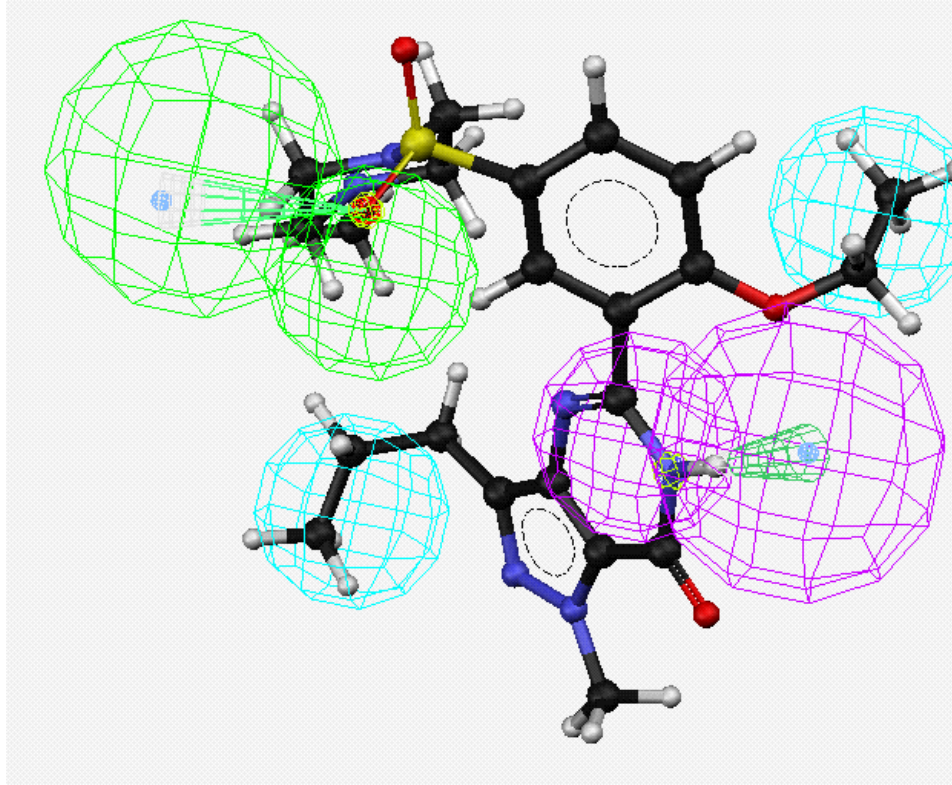
87
compounds

Farmakofor Analizleri

IC₅₀ 27nM

Biogen-Idec

Sildenafil Farmakofor Modeline uygulanarak bulunmuştur.



Ekins, S. *et al. Pharmacophore Perception, Development and Use in Drug Design*, Güner, O. F., Ed., **2000**, La Jolla, pp 269-288.