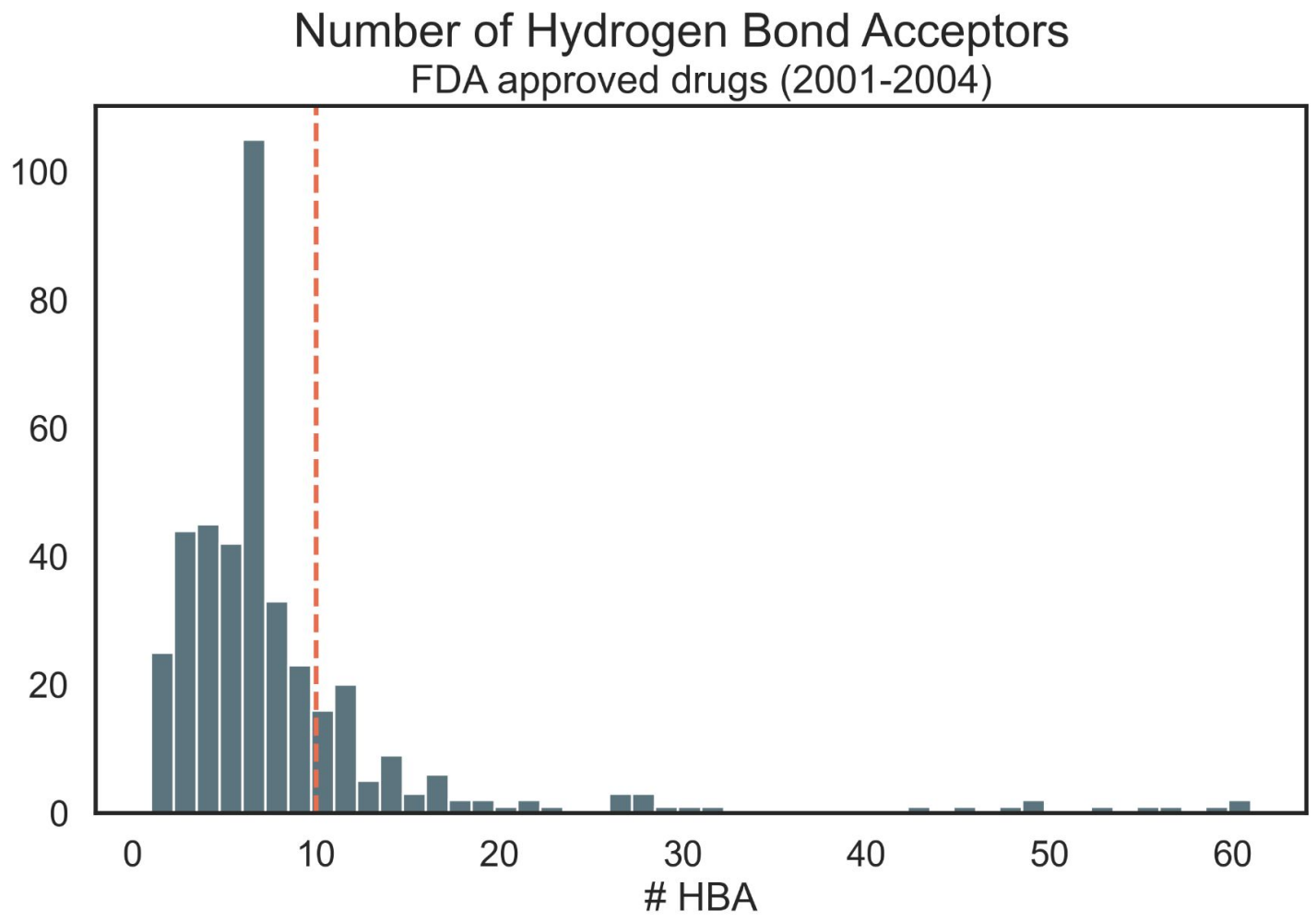
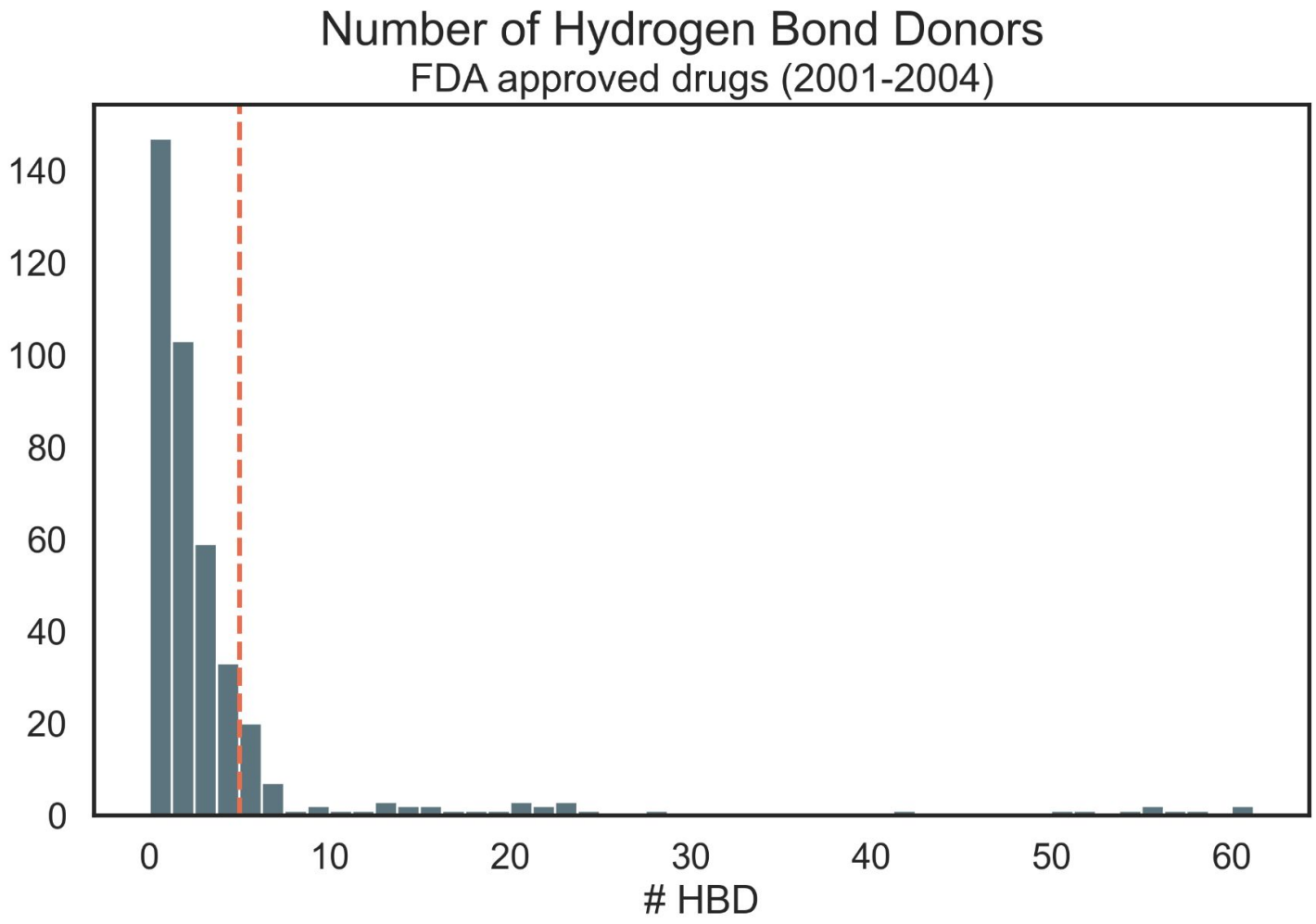
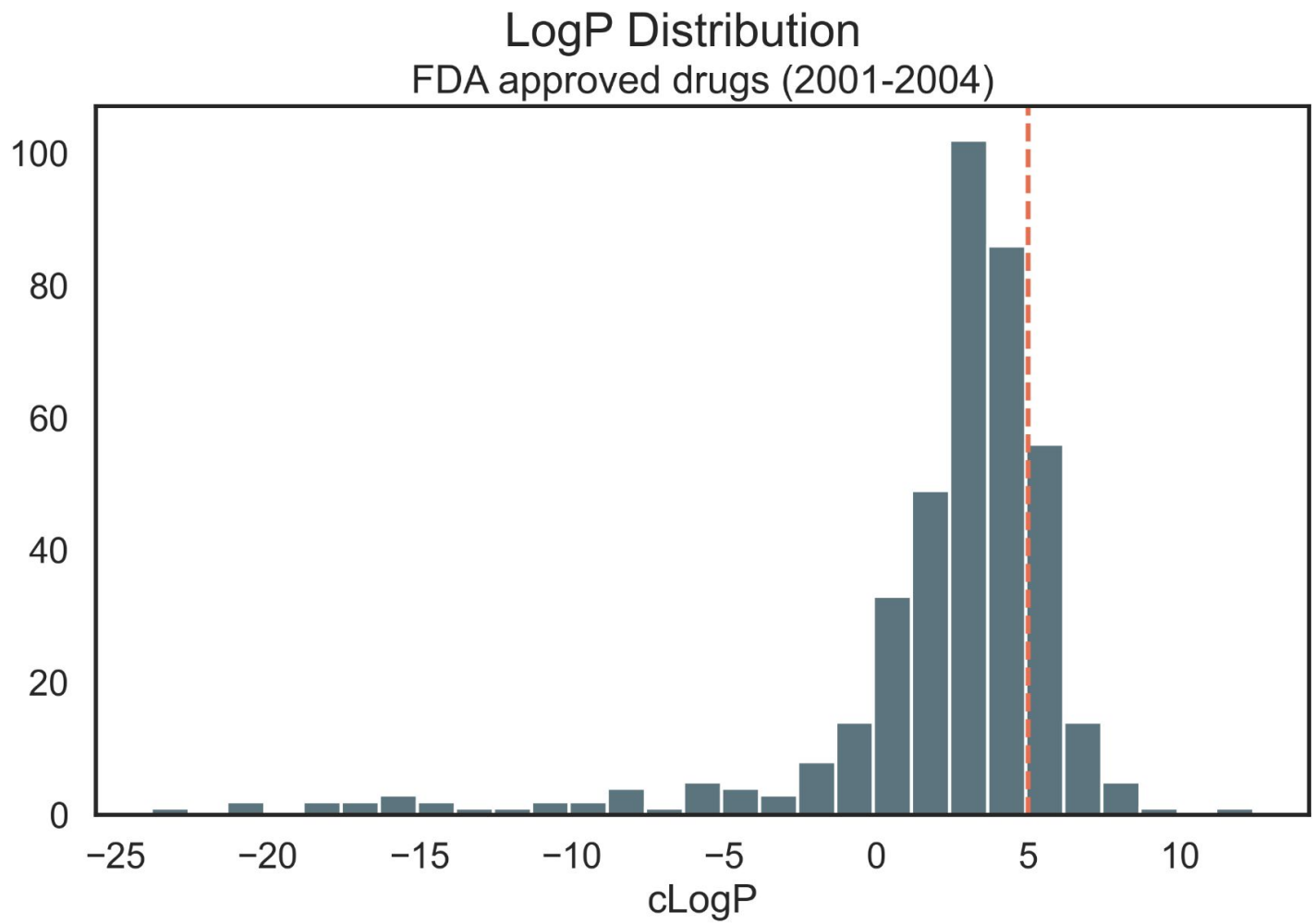
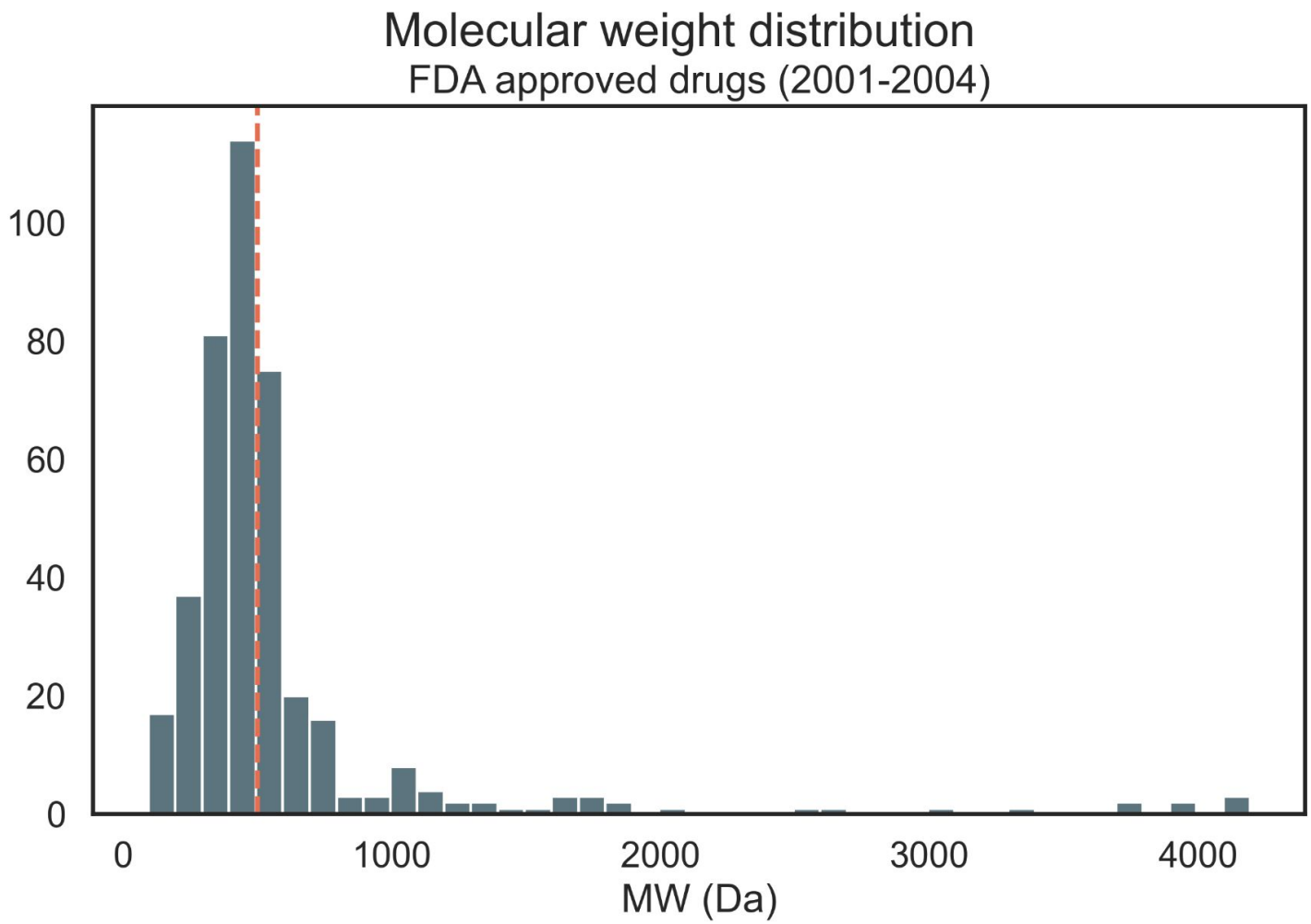
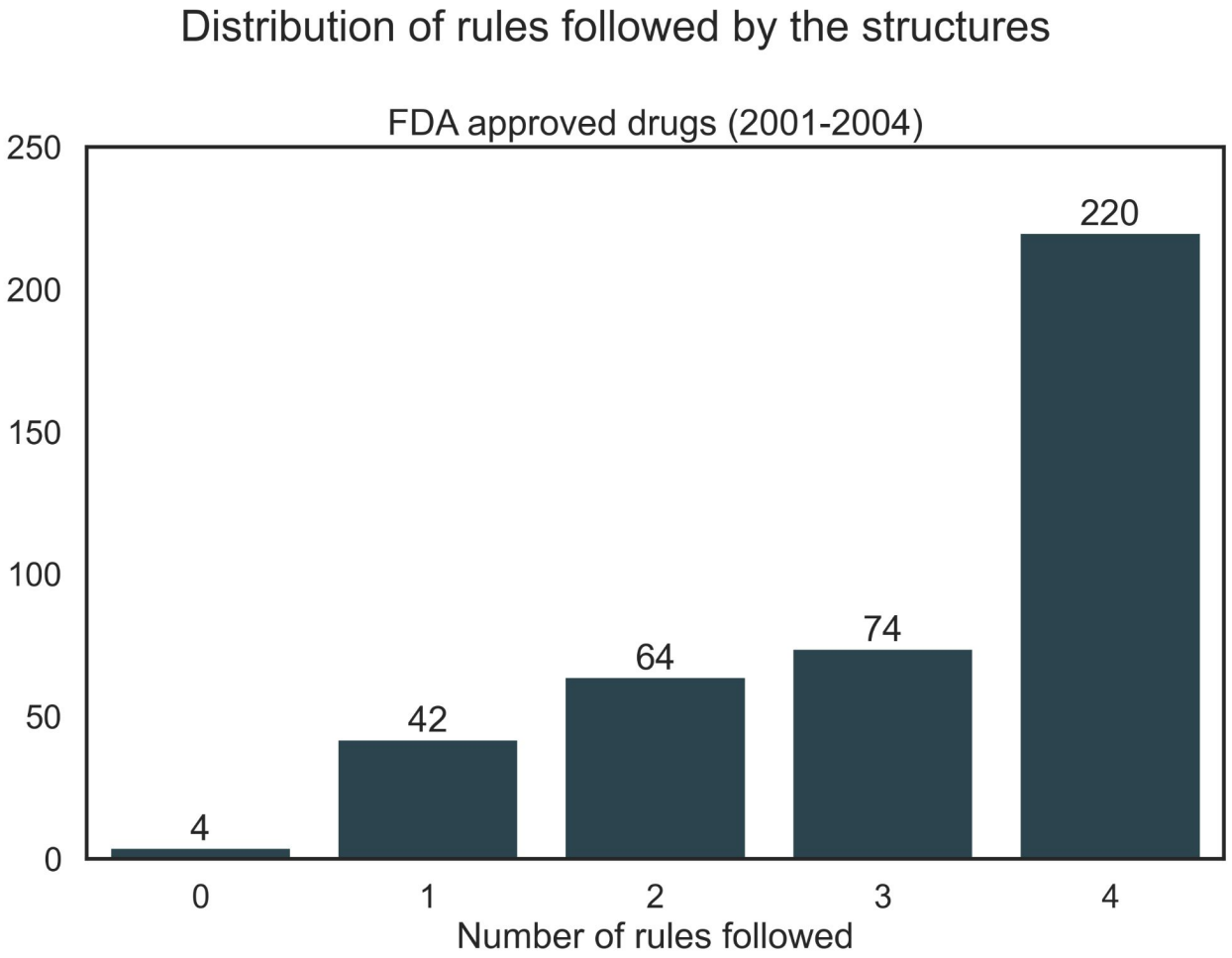
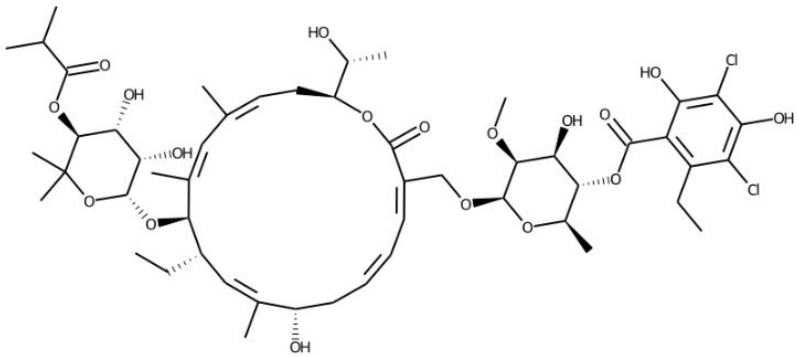

Number of Hydrogen Bond Acceptors
FDA approved drugs (2001-2004)
100
80
60
40
20
0
0
10
20
30
40
50
60
HBA


Number of Hydrogen Bond Donors
FDA approved drugs (2001-2004)
140
120
100
80
60
40
20
0
0
10
20
30
40
50
60
HBD

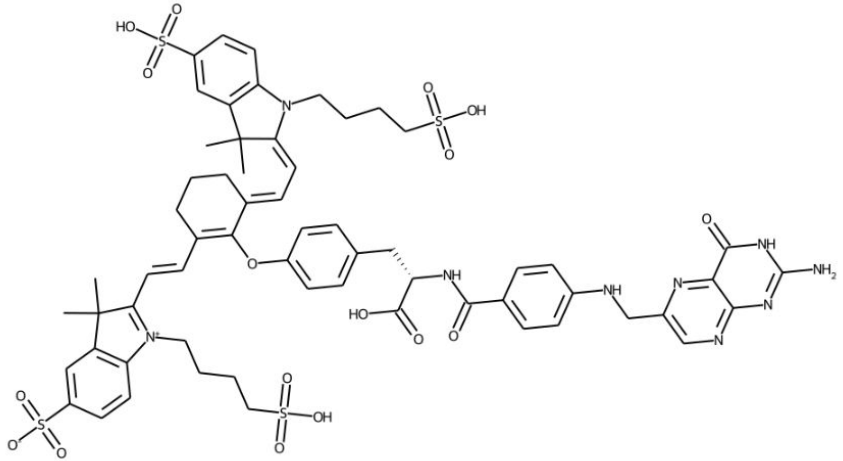

LogP Distribution
FDA approved drugs (2001-2004)
100
80
60
40
20
0
−25
−20
−15
−10
−5
0
5
10
cLogP


Molecular weight distribution
FDA approved drugs (2001-2004)
100
80
60
40
20
0
0
1000
2000
3000
4000
MW (Da)

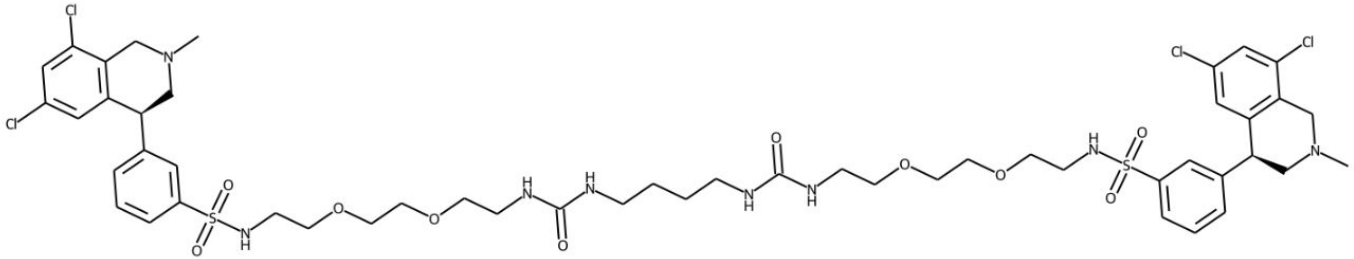

Distribution of rules followed by the structures
FDA approved drugs (2001-2004)
250
200
150
100
50
0
4
42
64
74
220
0
1
2
3
4
Number of rules followed



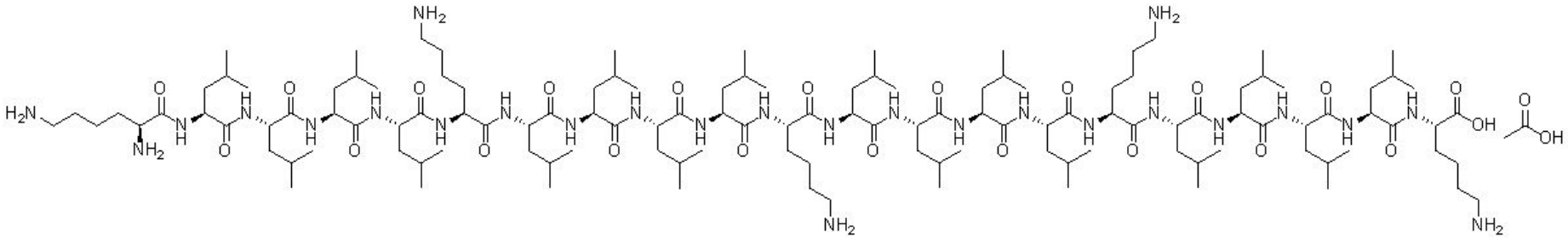
fidaxomicin



pafolacianine



tenapanor



lucinactant ??? + outras moléculas

Discussão de Resultados

Projeto Lipinski

Gustavo Henrique Marques Sousa

Artur Caminero Soares Gomes

Agosto, 2022

Análise de Fármacos Sintéticos Aprovados pelo FDA (1997-2021)

Perguntas:

- ➔ Os fármacos aprovados após a publicação da regra dos cinco de Lipinski seguem tais regras? Pode ser visto de outra forma: Qual o impacto das regras de Lipinski sobre o desenvolvimento de novos fármacos/candidatos à fármaco?
- ➔ Quantos (não) seguem?
- ➔ Como estão distribuídos?

Litec

Análise de Fármacos Sintéticos Aprovados pelo FDA (1997-2021)

Lipinski's Rule of Five (Ro5):

- Published on paper in **1997** and published online in **2001**
- Has almost 23.000 citations
- A molecular mass **less than 500 Daltons**
- **No more than 5 hydrogen bond donors** (the total number of nitrogen–hydrogen and oxygen–hydrogen bonds)
- **No more than 10 hydrogen bond acceptors** (all nitrogen or oxygen atoms)
- An octanol-water partition coefficient (**log P**) **less than 5**

Christopher A. Lipinski, Franco Lombardo, Beryl W. Dominy, Paul J. Feeney, Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings, Advanced Drug Delivery Reviews, Volume 23, Issues 1–3, 1997,

Link for access: <Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings>

Litec

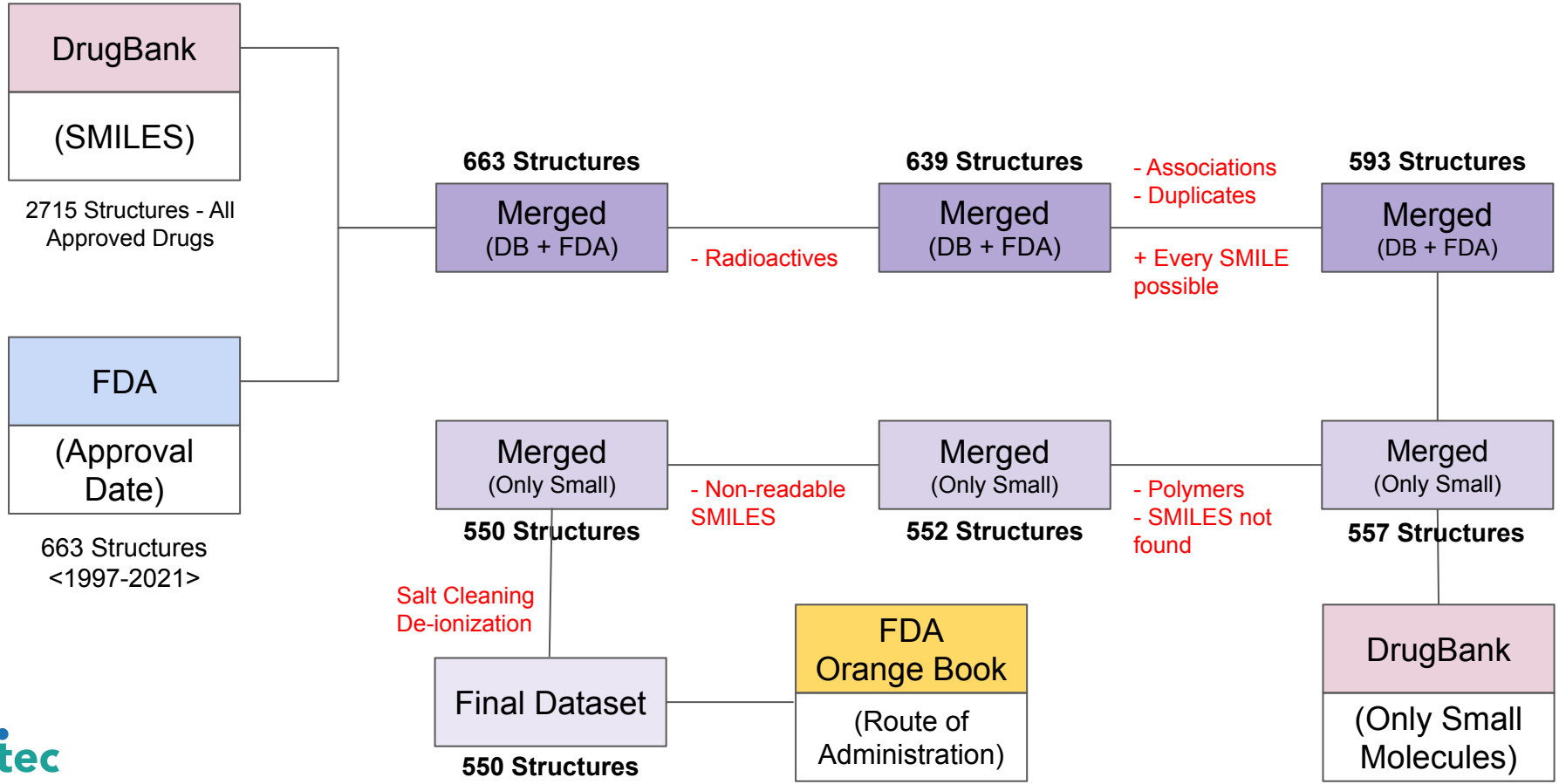
Análise de Fármacos Sintéticos Aprovados pelo FDA (1997-2021)

Procedimento de coleta de dados e curadoria:

- Approved Drugs(Drug Bank) = (**2715** structures)
- Data retrieved from FDA Access Data (Manual Downloaded): Compilation of CDER New Molecular Entity (NME)
- Raw from FDA 1997-2021 - (**663** structures - only Synthetic Ones)
- After we removed the radioactive structures - (**639** Structures)
- After we removed the associations and duplicates and manually retrieving every SMILE possible- (**593** Structures)
- Dataset retrieved from DrugBank with only small molecules
- After dropping what is not a small molecule - (**560** Structures)
- After dropping biological molecules and polymers- (**557** Structures)
- Removing SMILES not found - (**552** Structures)
- Dropping non-readable SMILES (**549** Structures)
- We did salt cleaning and deionization on all the structures

Litec

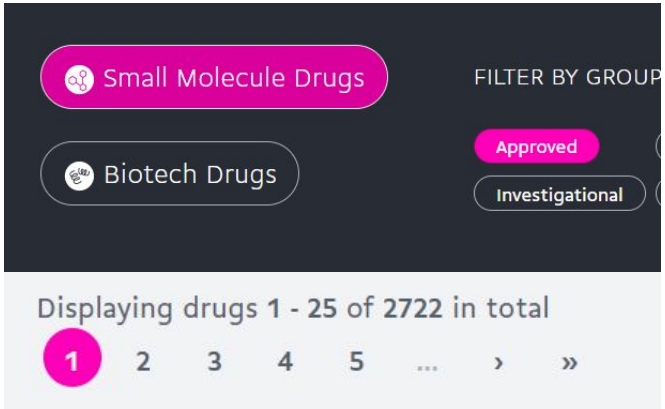
Análise de Fármacos Sintéticos Aprovados pelo FDA (1997-2021)



Litec

Análise de Fármacos Sintéticos Aprovados pelo FDA (1997-2021)

DRUGBANK Online



FDA U.S. FOOD & DRUG ADMINISTRATION

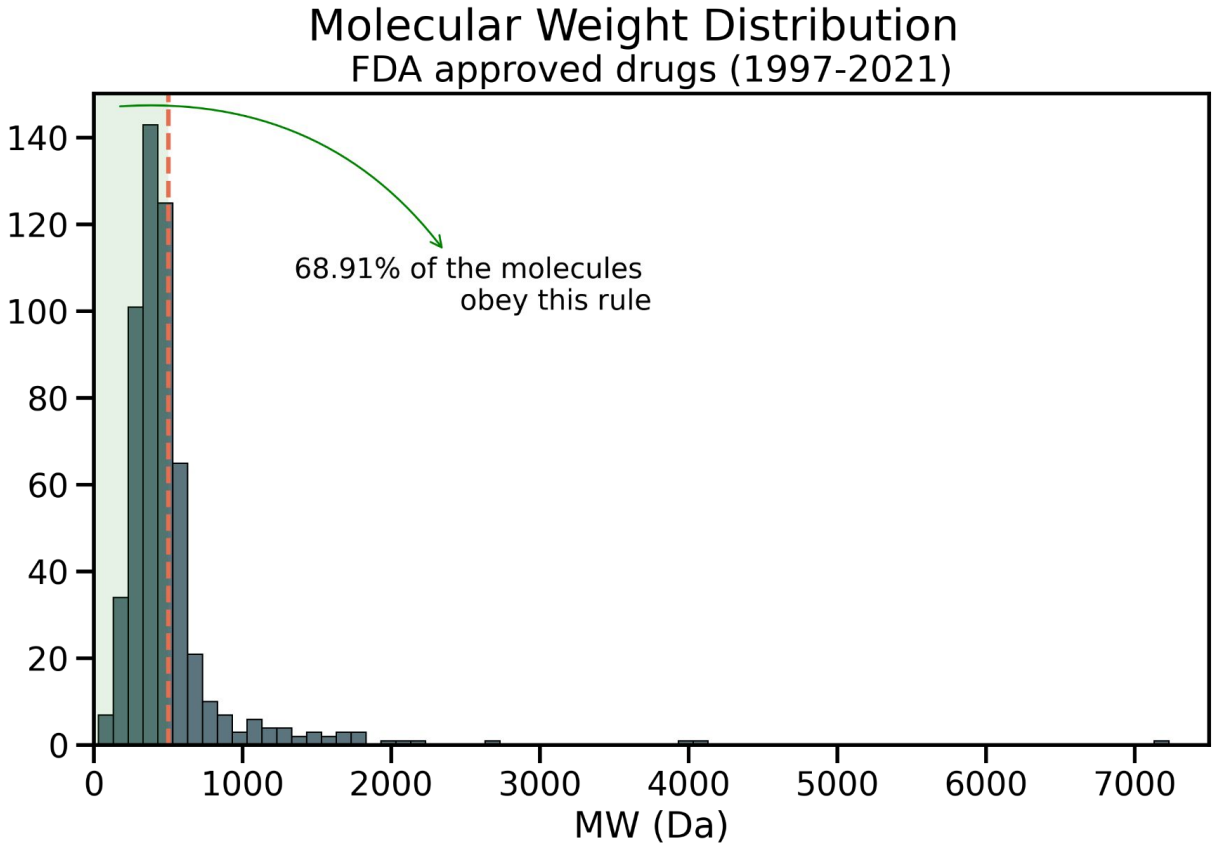
Compilation Dataset Links

- Compilation of CDER NME and New Biologic Approvals 1985-2021
- Compilation of CDER New Molecular Entity (NME) Drug and New Biologic Approvals - Data Dictionary (March 2022 PDF - 223KB)

DISCLAIMER: This dataset provides publicly available data on CDER NME and new biologic approvals (1985-2021) in a single-file, analyzable and user-friendly format. This dataset is for research purposes only and some fields have been simplified for ease of presentation. This dataset is a high-level compilation of existing, publicly available data from FDA's internal databases and document records, and to the best of our knowledge, reflects the state of each application at the time of initial regulatory approval. The agency aims to provide accurate information in this dataset and on this website. If you believe there is a factual error in the information presented, you can report this to CDER.NMENewBiologicApprovals@fda.hhs.gov.

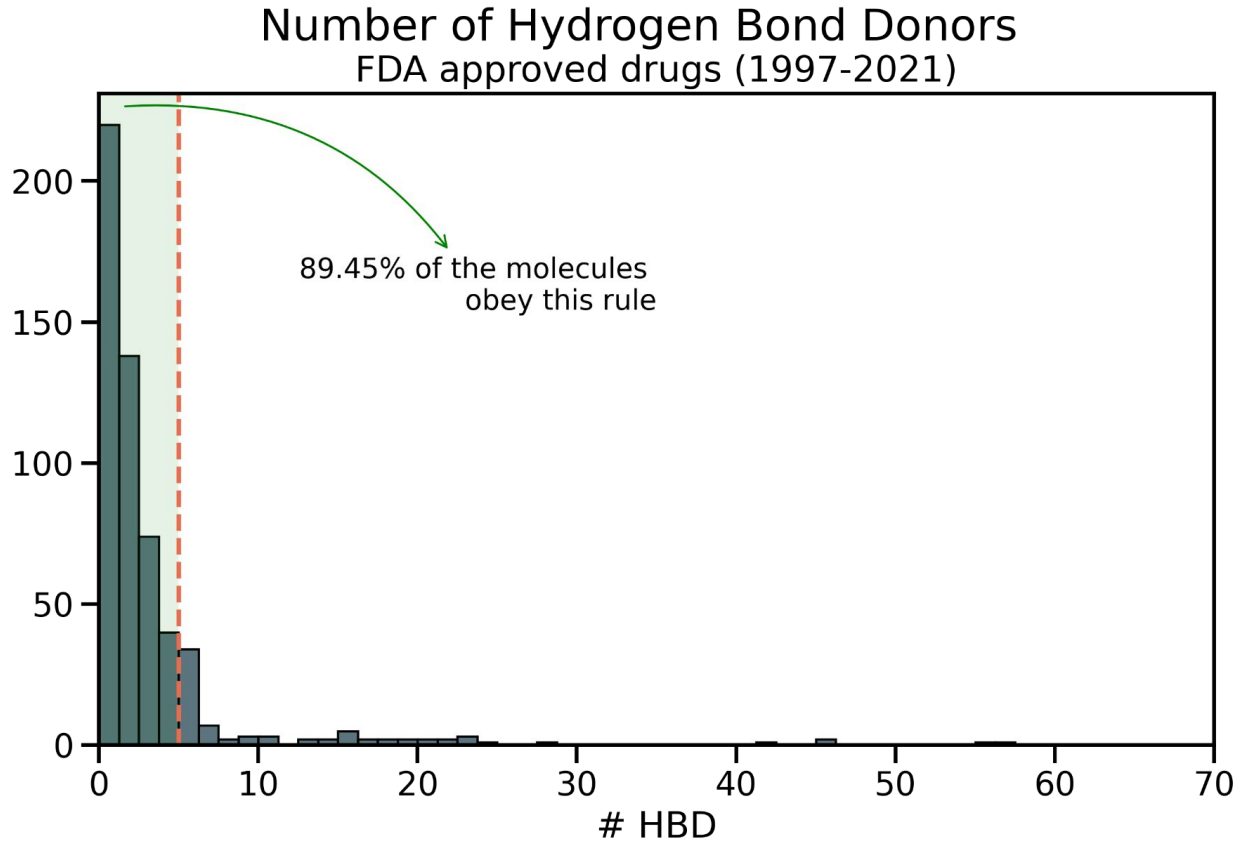
Litec

Análise de Fármacos Sintéticos Aprovados pelo FDA (1997-2021)



Litec

Análise de Fármacos Sintéticos Aprovados pelo FDA (1997-2021)



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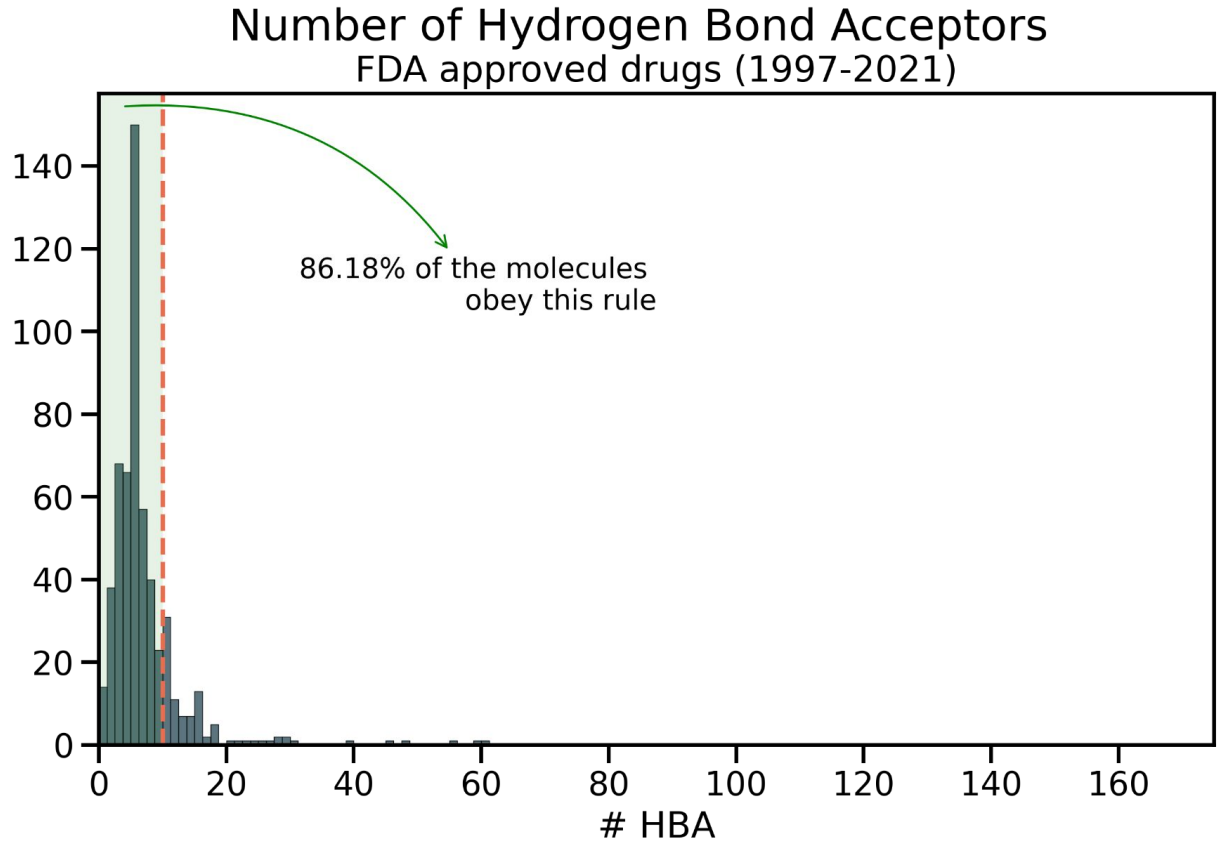
Análise de Fármacos Sintéticos Aprovados pelo FDA (1997-2021)



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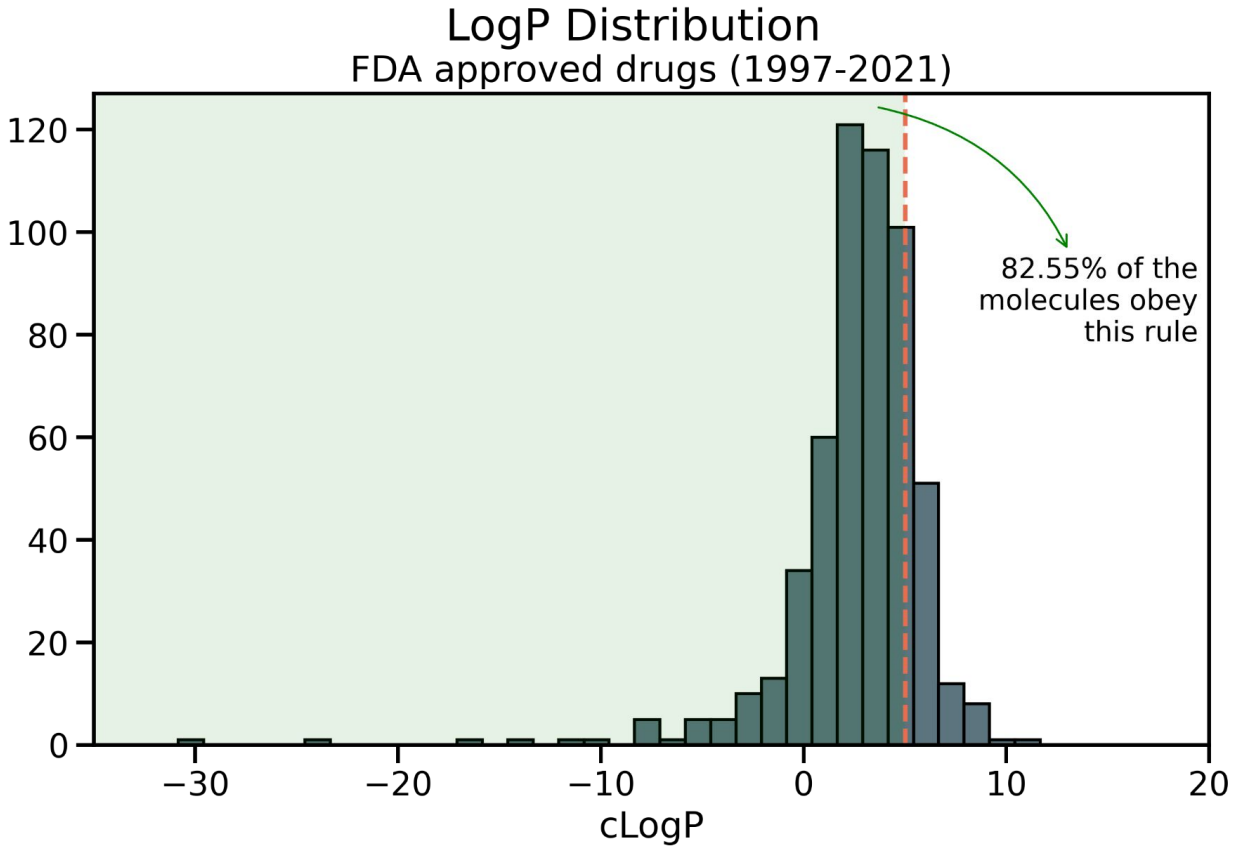

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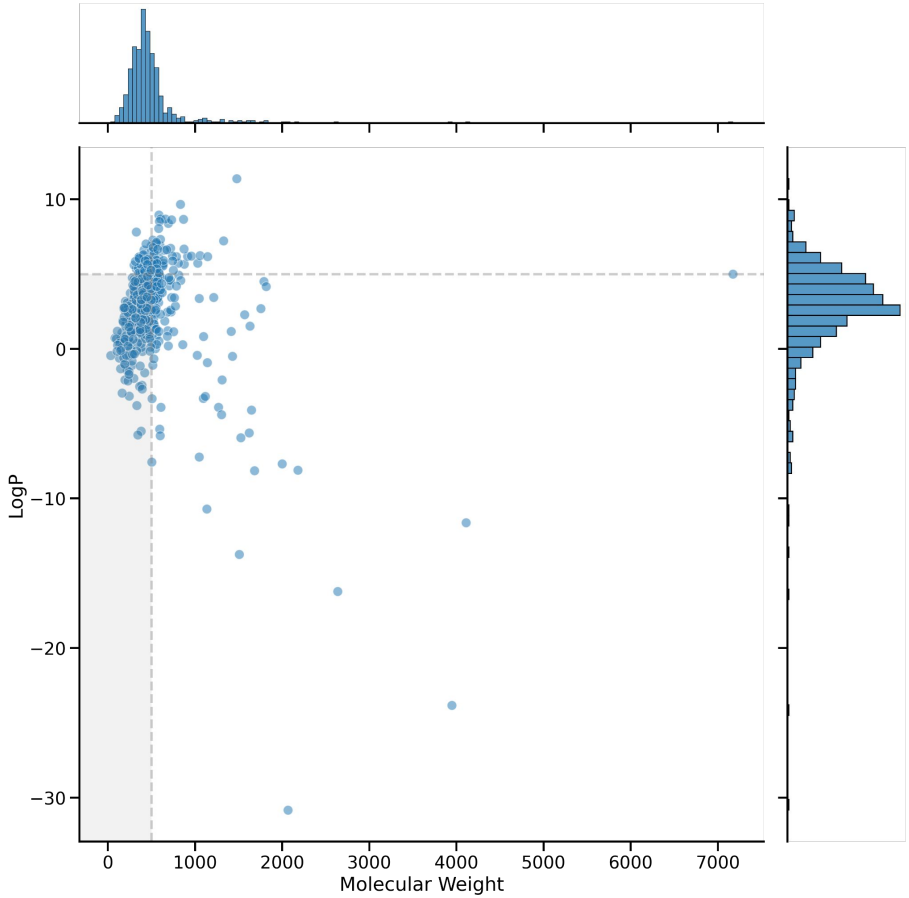
Análise de Fármacos Sintéticos Aprovados pelo FDA (1997-2021)



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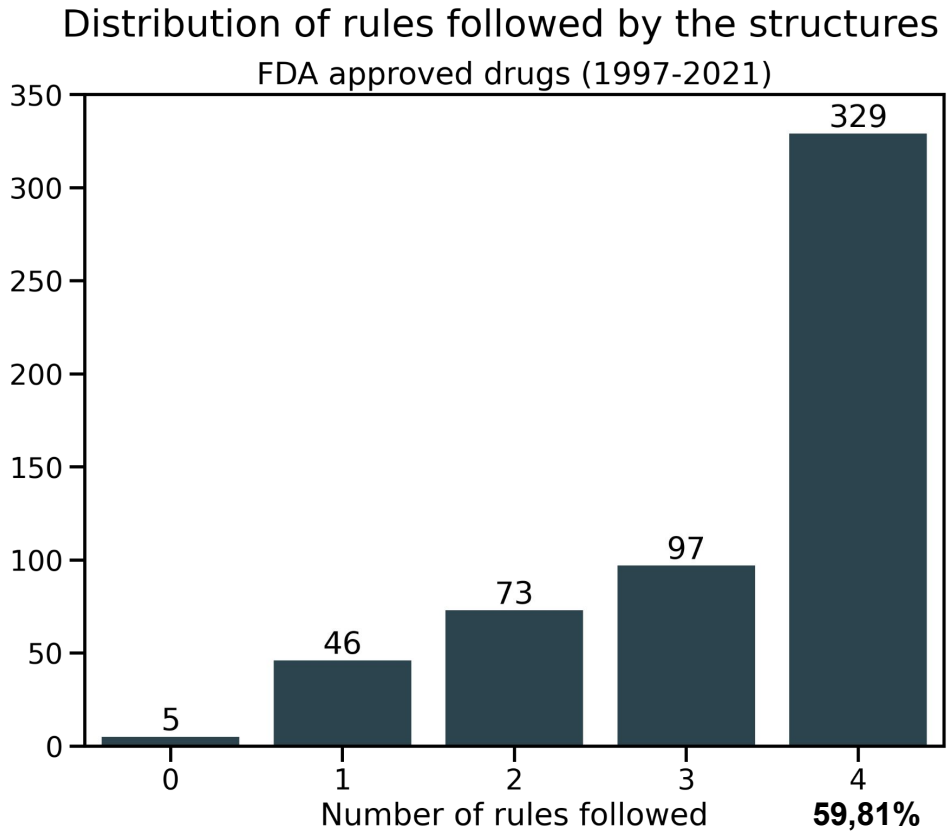
Análise de Fármacos Sintéticos Aprovados pelo FDA (1997-2021)



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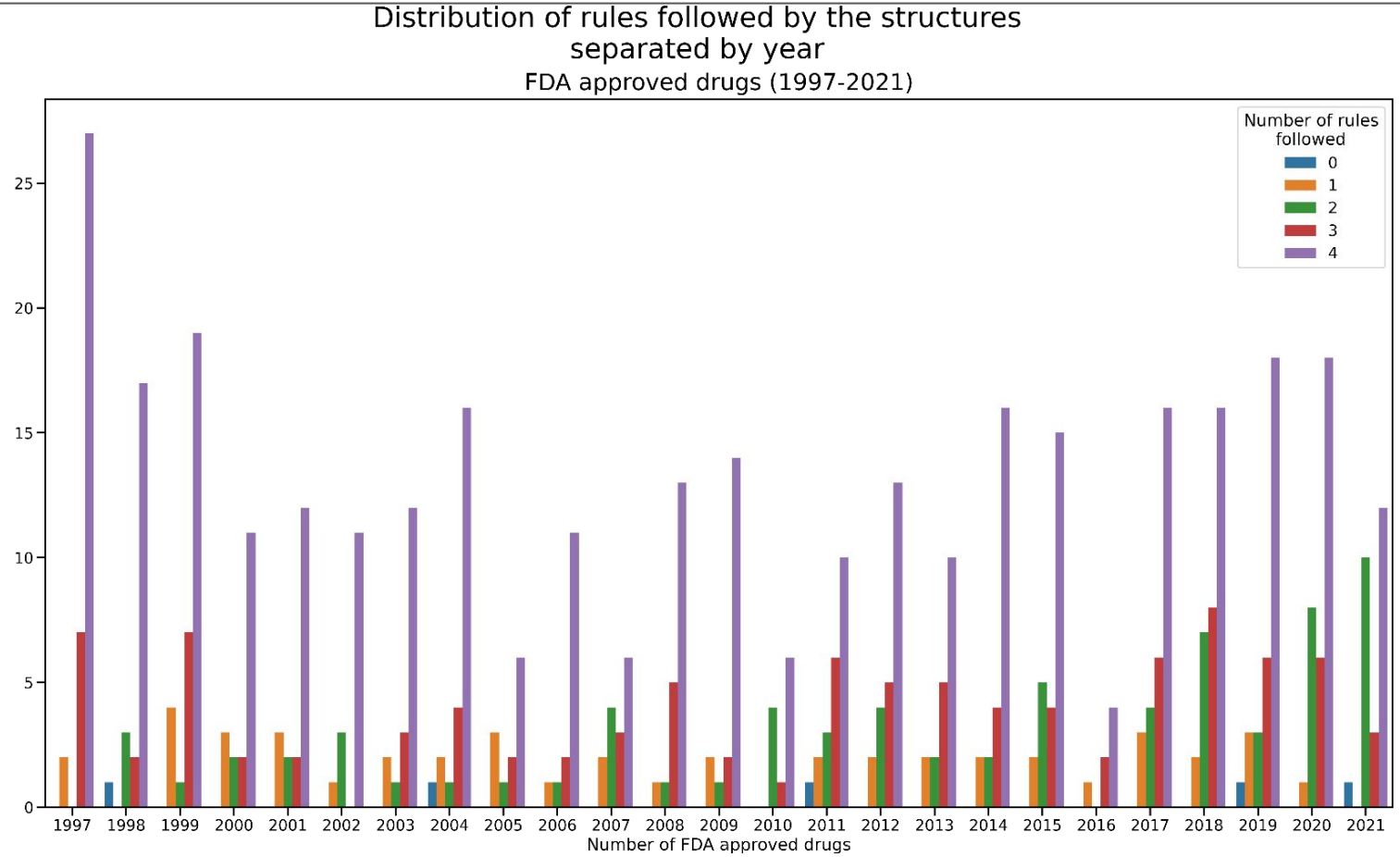
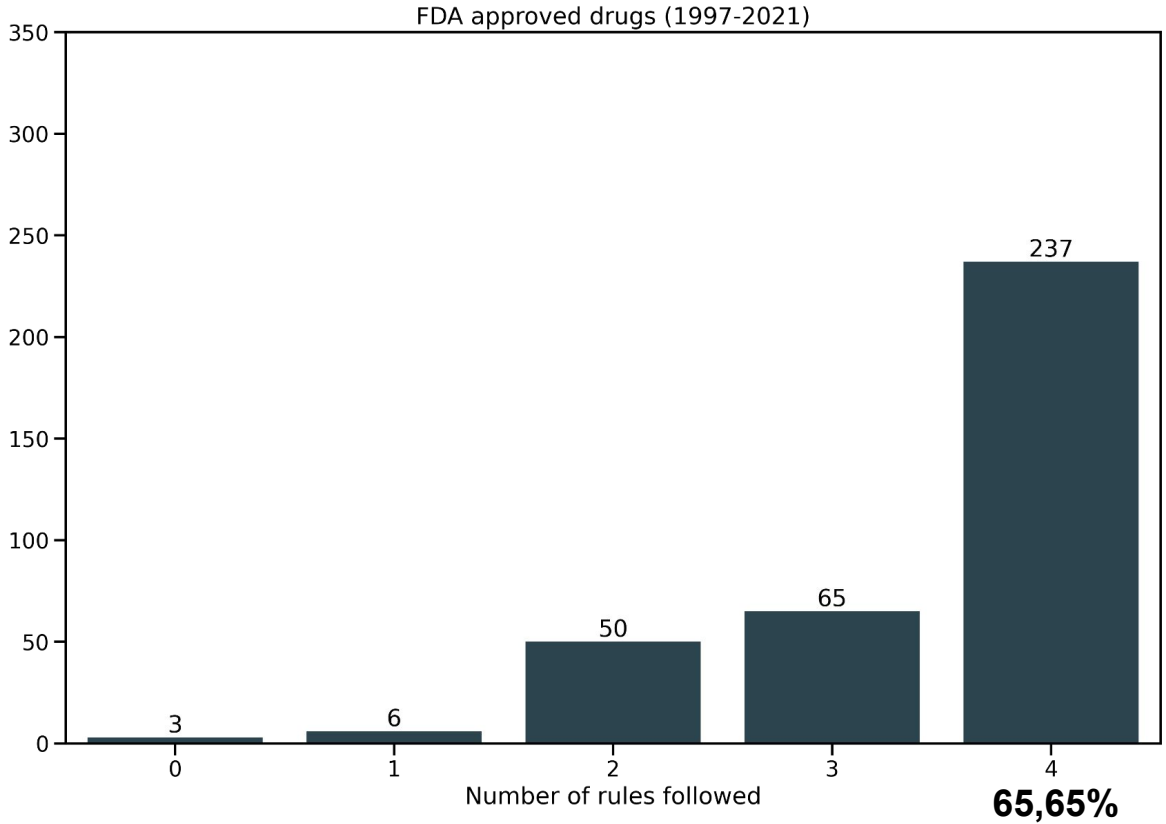
Análise de Fármacos Sintéticos Aprovados pelo FDA (1997-2021)



Litec

Análise de Fármacos Sintéticos Aprovados pelo FDA (1997-2021)

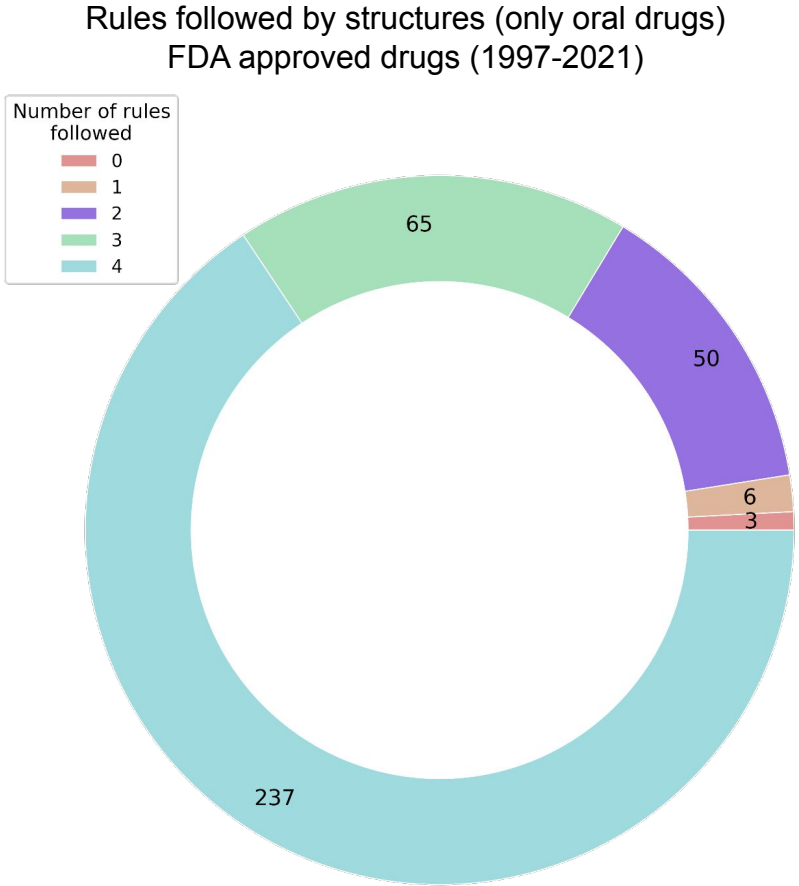
Distribution of rules followed by the structures (only oral drugs)



65,65%

Litec

Análise de Fármacos Sintéticos Aprovados pelo FDA (1997-2021)



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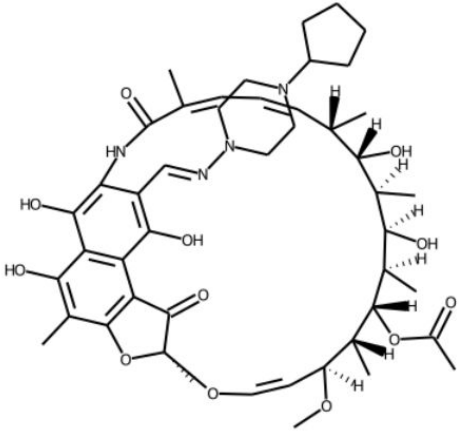
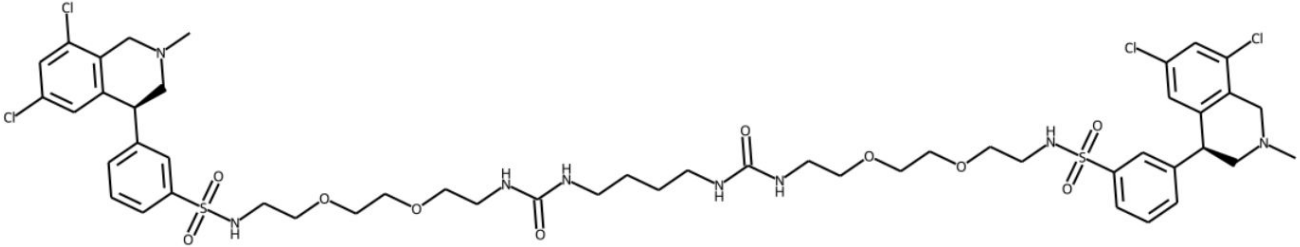
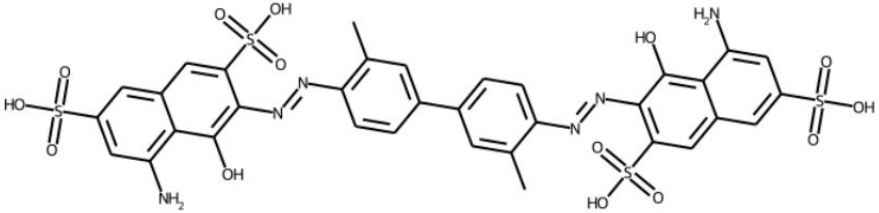
Análise de Fármacos Sintéticos Aprovados pelo FDA (1997-2021)



rifapentine
(oral)



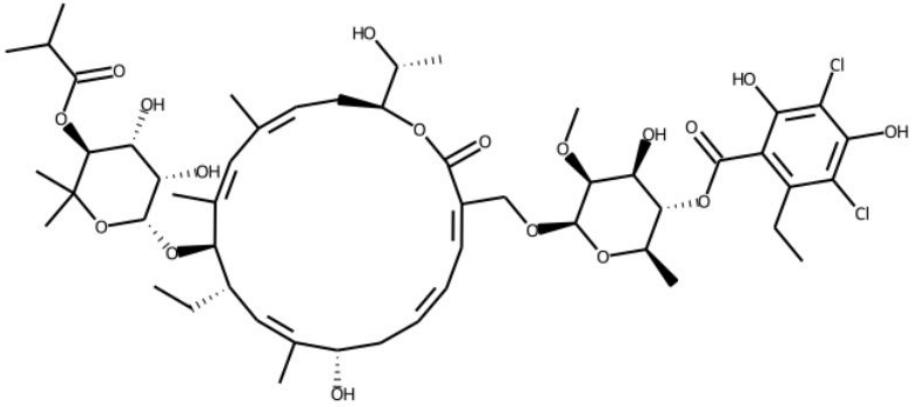
tenapanor
(oral)



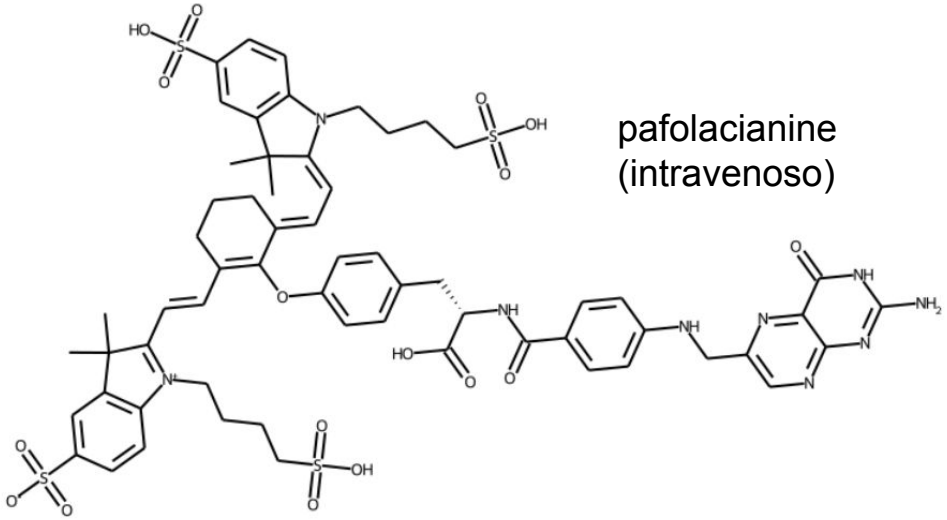
trypan blue
(oftálmico)

Litec

Análise de Fármacos Sintéticos Aprovados pelo FDA (1997-2021)



fidaxomicin
(oral)



pafolacianine
(intravenoso)

Litec