Quantitative Structure-Activity Relationship (QSAR) Analysis Of Antileishmanial Natural Products

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INTRODUCTION AND BACKGROUND

Leishmanieses are diseases transmitted from sandflies to humans. These diseases account for 12 million infections worldwide. There are several manifestations of leishmaniasis and the results of can range from lesions on the skin to permanent spleen and liver damage. If untreated the effects of this disease can be fatal. There is no vaccine available and the current treatments have adverse side effects. Extensive research on the effects on natural products and their effects on *Leishmania* protein targets. For my research project I compiled bioactivity data collected in aforementioned studies and attempted to relate said data with numerous descriptors for use in QSAR programs.

PROCEDURE

After compiling all of the bioactivity data into an organized spreadsheet that data as well as the molecular structure of the particular compound had to be recorded into a database within MOE (Molecular Operating Environment). MOE then generated a list of compound specific descriptors. After the descriptors are generated the next task was to determine if there was a correlation between the descriptors and the predetermined biological activities.

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	species	compound	ic-50(uM)	vd
1	L. peruviana (P	penta-O-acetylq	11.1800	482.3724
2	L. peruviana (P	hepta-O-acetylt	10.5300	680.6676
3	L. peruviana (P	octa-O-acetylhy	7.3500	749.9362
4	L. braziliensis	hepta-O-acetylt	8.7200	680.6676
5	L. braziliensis	octa-O-acetylhy	6.2100	749.9362
6	L. braziliensis	3-(3,7-dimethyl	22.3000	534.5500
7	L. braziliensis	pentamidine	29.4000	884.2234
8	L. braziliensis	"methyl 3,4-dih	58.4000	231.3137
9	L. braziliensis	flavokavain B	11.2000	730.5591
10	L. donovani (P)	machilin-G	50.5000	263.4356
11	L. donovani (P)	5-acetyl-4-hydr	10.7000	563.2231
12	L. donovani (P)	"methyl 3,4-dih	78.4000	152.7440
13	L. donovani (P)	Malabaricone A	49.0000	178.6694
14	L. donovani (P)	Malabaricone B	64.2000	683.7650
15	L. donovani (P)	flavokavain B	11.2000	570.3400
16	L. donovani (P)	Calceolarioside	41.8000	745.1004
17	L. donovani (A)	5-(110(S)-Hydro	7.0000	133.4523
18	L. donovani (A)	"5-(12'(S)-hydr	3.0000	395.0091
19	L. donovani (A)	5,7,3',4'- tetr	13.0000	732.2254

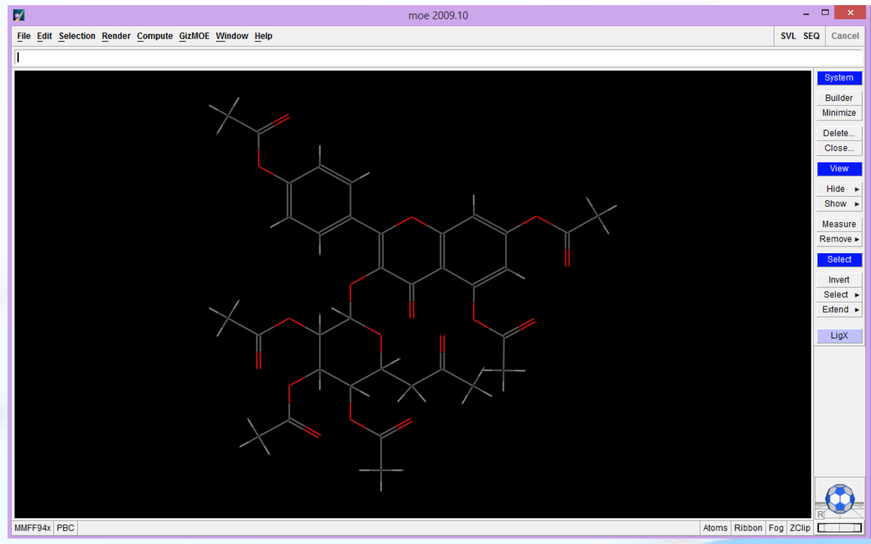
DESCRIPTORS

Within MOE different databases were created for each type of compound (alkaloids, phenolics, quinones, etc.). The compounds were then sorted by the species of *Leishmania* tested as well as the life cycle stage specified. After the molecules were constructed using MOE the following descriptors were computed:

- Principal moments of inertia
- Vander Walls surface area
- Polar surface area
- Number of hydrogen acceptor and donor atoms
- Number of basic, acidic, and hydrophobic atoms
- Various electronic descriptors (HOMO, LUMO, dipole moment.

CONCLUSION

The goal of this project was to determine a correlation between biological activity and QSAR descriptors. After obtaining all of the numerical descriptors I compared those values to the IC_{50} values by graphical means to compare possible trends. I also used features of the MOE software to see possible correlations and there were none I could find.



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