

Supplemental material

In Silico ADME/Tox Profiling of natural products: a Focus on BIOFACQUIM

Noemi Angeles Durán-Iturbide, Bárbara I. Díaz-Eufracio*, José L. Medina-Franco*

School of Chemistry, Department of Pharmacy, National Autonomous University of Mexico, Avenida Universidad 3000, 04510 Mexico City, Mexico

*Correspondence: dieb@comunidad.unam.mx (Díaz-Eufracio); medinajl@unam.com.mx (Medina-Franco);
Tel.: +5255-5622-3899

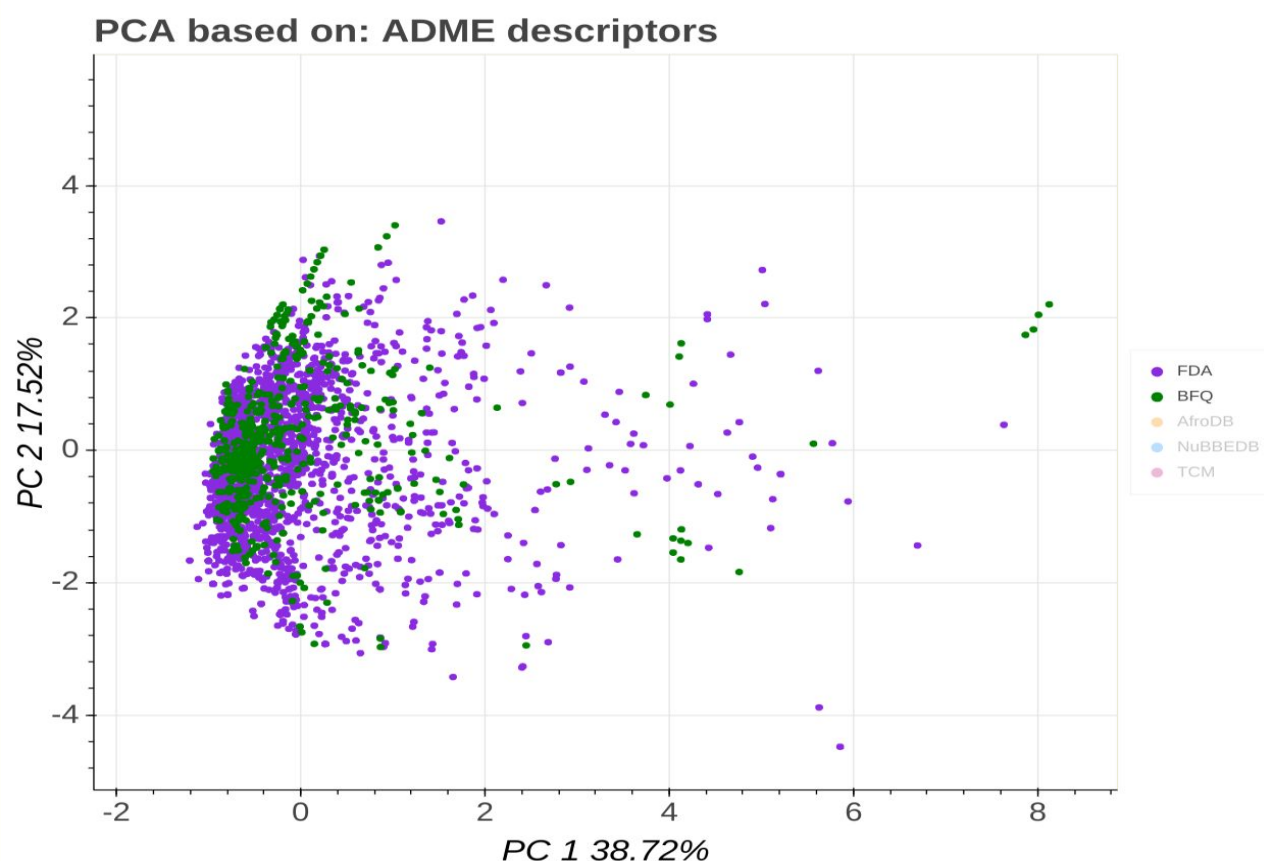


Figure S1. Chemical Space visualization of BIOFACQUIM and FDA datasets

Table S1. PCA summary.

	PC 1	PC 2
Percentage of variance	0.38	0.18
Cumulative percentage of variance	0.38	0.56

Table S2. PCA loadings.

	PC 1	PC 2	PC 3
MW	0.32	0.19	-0.19
#Rotatable Bonds	0.29	0.08	0.16
#Acceptors	0.33	-0.15	0.25
#Donors	0.33	-0.19	0.22
Surface Area	0.35	0.07	0.25
Silicos-IT LogSw	-0.01	-0.46	-0.34
Consensus Log P	-0.07	0.48	0.23
Intestinal absorption	-0.27	0.28	-0.04
BBB permeability	-0.33	0.17	-0.20
Fraction unbound	0.02	-0.39	-0.17
Total Clearance	-0.13	0.05	-0.19
Fraction Csp3	0.09	0.07	-0.36
#Heavy atoms	0.32	0.21	-0.18
Lipinski #violations	0.26	0.13	-0.38
Veber #violations	0.26	0.06	-0.39
Leadlikeness #violations	0.15	0.35	-0.16

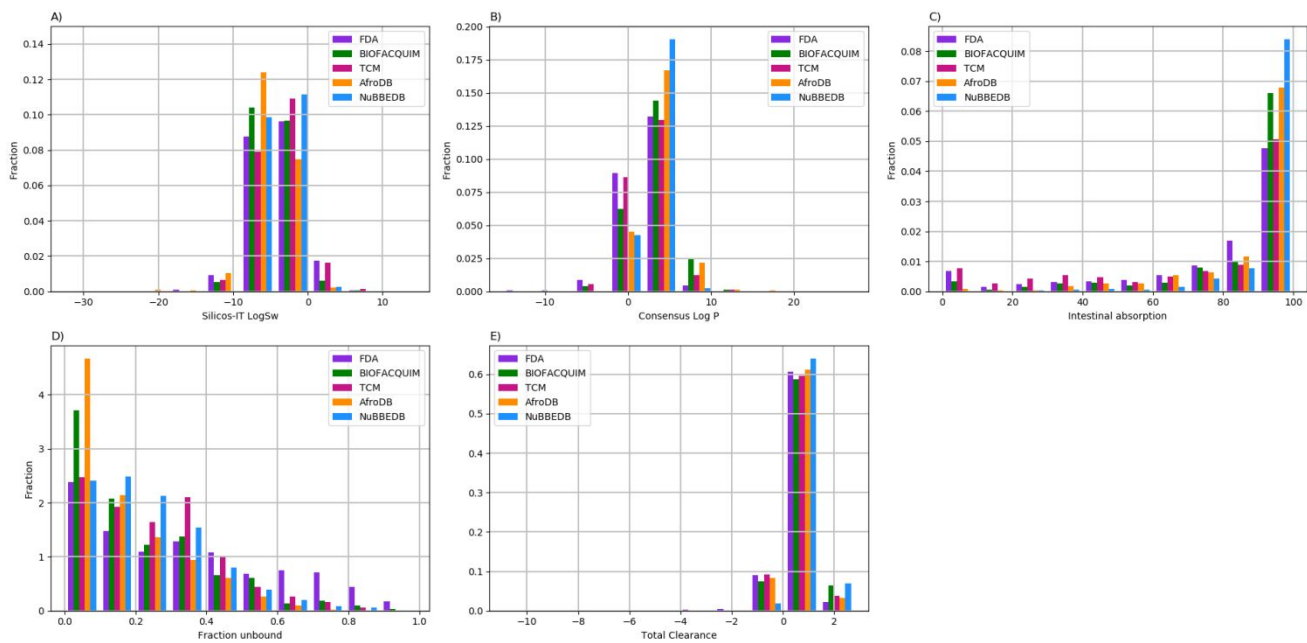


Figure S2. Histograms A)Silicos -IT LogSW, B)Consensus Log P, C)Intestinal absorption, D)Fraction unbound and E)Total clearance

Table S3. Statistical values of Silicos-IT LogSW predicted with SwissADME.

Database	mean	std	min	25%	50%	75%	max
AfroDB	-5.171	2.643	-20.61	-6.478	-5.03	-3.618	4.02
BIOFACQUIM	-4.197	2.611	-13.44	-5.63	-4.4	-2.675	6.4
FDA	-3.996	3.216	-19.66	-5.86	-4.105	-2.14	14.44
NuBBE _{DB}	-4.007	1.642	-8.47	-5.1	-4.22	-3.03	3.67
TCM	-3.627	2.996	-32.55	-5.36	-3.64	-1.92	8.92

Table S4. Statistical values of Consensus LogP predicted with SwissADME.

Library	mean	std	min	25%	50%	75%	max
AfroDB	3.541	2.246	-2.23	2.202	3.35	4.588	20.2
BIOFACQUIM	2.993	2.329	-6.41	1.745	2.76	3.93	12.1
FDA	1.949	2.412	-15.01	0.638	2.275	3.51	11.9
NuBBE _{DB}	2.916	1.334	-3.38	2.16	2.8	3.72	7.9
TCM	2.45	2.531	-6.87	1.02	2.45	3.72	27.31

Table S5. Statistical values of intestinal absorption in humans predicted with pkCSM-pharmacokinetics.

Library	mean	std	min	25%	50%	75%	max
AfroDB	86.934	17.887	0	84.364	94.236	97.324	100
BIOFACQUIM	83.433	23.57	0	81.087	93.61	96.304	100
FDA	75.458	28.327	0	66.876	89.224	93.864	100
NuBBEDB	92.241	10.679	9.754	92.549	95.076	97.061	100
TCM	72.288	31.79	0	49.364	90.5	95.879	100

Table S6. Percentage of common distribution endpoints prediction.

variable	FDA	BIOFACQUIM	AfroDB	NuBBE _{DB}	TCM
BBB permeability	39	41	36	70	30
Pgp substrate	41	29	37	18	47

Table S7. Statistical values of fraction unbound predicted with pkCSM-pharmacokinetics.

Library	mean	std	min	25%	50%	75%	max
AfroDB	0.158	0.154	0	0.026	0.114	0.244	0.76
BIOFACQUIM	0.213	0.201	0	0.047	0.148	0.332	0.969
FDA	0.339	0.261	0	0.106	0.307	0.53	0.987
NuBBE _{DB}	0.233	0.167	0	0.104	0.208	0.333	0.989
TCM	0.253	0.186	0	0.1	0.237	0.379	0.933

Table S8. Percentage of CYP inhibition by dataset.

	Percentage CYPs inhibition				
	FDA	BIOFACQUIM	AfroDB	NuBBE _{DB}	TCM
CYP1A2	21	30	27	47	19
CYP2C19	18	22	26	33	14
CYP2C9	20	31	38	37	20
CYP2D6	30	22	31	36	18
CYP3A4	24	30	41	31	23

Table S9. Statistical metrics of Total Clearance predicted with pkCSM-pharmacokinetics.

Library	mean	std	min	25%	50%	75%	max
AfroDB	0.5	0.477	-2.689	0.196	0.458	0.73	2.547
BIOFACQUIM	0.605	0.521	-2.458	0.238	0.565	0.861	2.078
FDA	0.505	0.689	-10.922	0.255	0.573	0.852	2.796
NuBBE _{DB}	0.705	0.465	-0.171	0.328	0.643	0.973	2.242
TCM	0.547	0.533	-5.197	0.221	0.519	0.823	2.56

Table S10. Percentage of common toxicity endpoints prediction.

variable	FDA	BIOFACQUIM	AfroDB	NuBBE _{DB}	TCM
hERG I inhibitor	2	0	0	0	0
hERG II inhibitor	31	28	45	21	37
AMES toxicity	16	19	22	25	17
Hepatotoxicity	74	15	20	15	15