Study of derivatives of natural products in their interaction against tubulin using in silico tools

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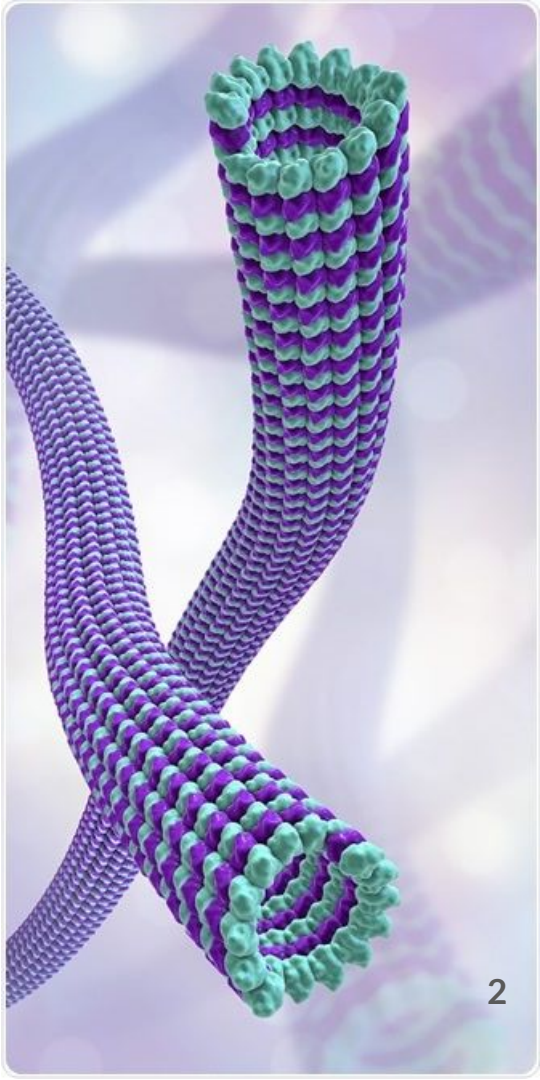
Context

- Cancer (cell proliferation)
- Cell migration (metastasis)
- Metabolic regulation
- Immune system regulation
- Etc.

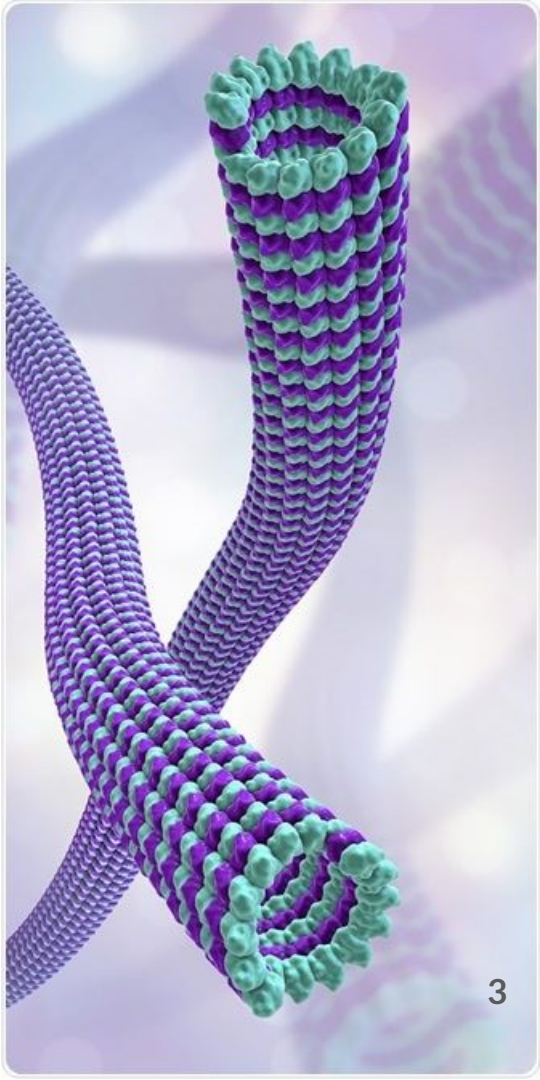


Sallee, M. D., & Feldman, J. L. *Current Biology*, ***2021***, *31(10), R506–R511.*

Main goals

- Identify compounds of natural and / or semisynthetic origin with a potential interaction on tubulin and / or microtubules.

- Prioritize the biological evaluation of potential tubulin/ microtubules inhibitors.



Methods

Benchmark database construction
(Based on cellular information)

Data curation

Chemical space analysis

Pharmacological profile (drug-like)

ADMET profile

Molecular modeling

Molecular docking

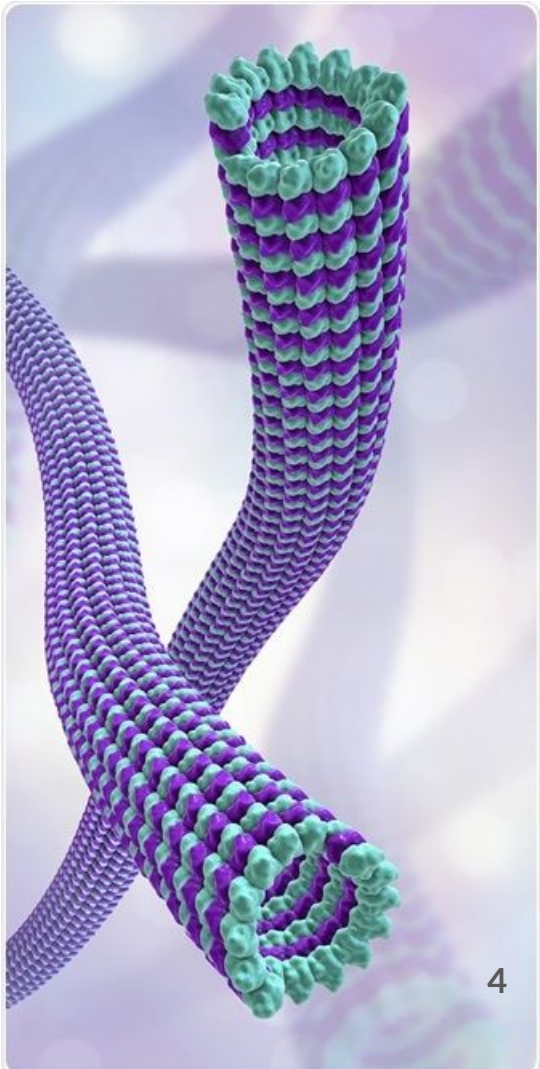
Pharmacophore modeling

Virtual screening of databases of natural products

Molecular dynamics

Binding energy prediction based on ML approach*

Final selection of compounds to evaluate (*in vitro*)



* Sánchez-Cruz N., Medina-Franco J.L., Mestres J., Barril X. *Bioinformatics*, **2021**, 37(10), 1376–1382.

Consensus Database

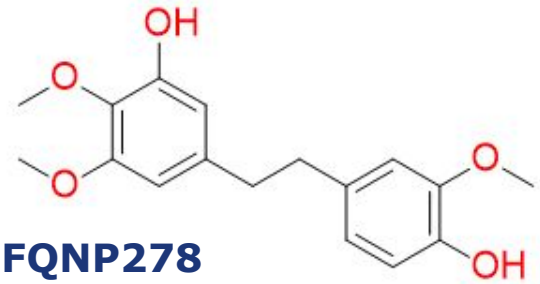
Violations of the rules of:
Lipinsky, Ghose, Veber, Egan and Muegge

A	B	C	D	E	F	G	H	I	J	K	L	M	N
ID	SMILES	Morgan si	MACCS	S	S_NonHAt	GI absorption	Pgp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibi	Violations
FQNP278	cc(c(c2)O	0.416667	0.8	-7.4708	-0.33958	High	No	Yes	No	Yes	Yes	No	0
FQNP310	ccc(c(c2)O	0.34	0.85714	-8.31432	-0.39592	High	No	Yes	Yes	No	Yes	No	0
FQNP362	c1oc(c1cc	0.355932	0.82352	-6.02001	-0.26174	High	No	Yes	No	Yes	Yes	Yes	0
FQNP443	OC)C(=O)	0.346939	0.82758	-7.8139	-0.37209	High	No	Yes	Yes	Yes	Yes	No	0
FQNP112	cc(=O)c2c	0.339623	0.82857	-7.68182	-0.30727	High	No	Yes	No	Yes	Yes	Yes	0
FQNP442	)(=O)OCc	0.333333	0.82758	-7.33175	-0.33326	High	No	Yes	Yes	No	Yes	No	0
FQNP110	1cc(=O)c	0.351852	0.77142	-6.84235	-0.31102	High	No	Yes	No	Yes	Yes	Yes	0
FQNP364	c(OC)c(c(	0.326531	0.82758	-6.24702	-0.28396	High	No	Yes	No	Yes	Yes	No	0
FQNP316	2c(c1O)c1	0.366667	0.74193	-6.82628	-0.34131	High	Yes	Yes	No	No	Yes	Yes	0
FQNP437	)(=O)OCc1	0.345455	0.76667	-6.69721	-0.31891	High	No	Yes	Yes	No	Yes	No	0
FQNP369	C)cc2c1c1	0.366667	0.74193	-5.14815	-0.25741	High	Yes	Yes	No	No	Yes	Yes	0
FQNP126	(c2c(c1O)	0.354839	0.75	-6.94245	-0.31557	High	Yes	Yes	No	No	Yes	Yes	0
FQNP113	c(=O)c2c	0.315789	0.8	-5.69147	-0.23714	High	No	Yes	No	Yes	Yes	Yes	0
FQNP1	2cc(O)c(c(	0.3	0.82857	-5.13893	-0.20556	High	No	Yes	No	Yes	Yes	Yes	0
FQNP440	COC(=O)c	0.316667	0.79310	-7.02377	-0.33447	High	No	Yes	Yes	Yes	Yes	No	0
FQNP361	O)c(O)cc(	0.305085	0.8	-7.3582	-0.31992	High	No	Yes	No	Yes	Yes	Yes	0
FQNP129	2ccc(c(c2)	0.320755	0.76666	-7.8377	-0.39189	High	No	Yes	No	No	Yes	No	0
FQNP223	1c(=O)c(c	0.305085	0.79411	-8.9103	-0.4243	High	No	Yes	No	No	Yes	Yes	0
FQNP280	3c2ccc(c3	0.333333	0.74193	-7.19851	-0.35993	High	Yes	Yes	No	No	Yes	Yes	0
FQNP439	1C(=O)OC	0.307692	0.75862	-4.87412	-0.24371	High	No	Yes	Yes	No	Yes	No	0
FQNP438	1COC(=O	0.322034	0.73333	-7.18635	-0.37823	High	No	Yes	Yes	Yes	No	No	0
FQNP165	1oc2cc(O	0.3	0.77142	-6.86472	-0.29847	High	No	Yes	No	No	Yes	Yes	0

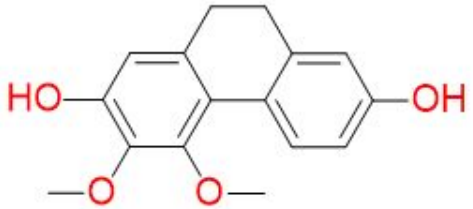
1 = Max. similarity
0 = Min. similarity

Negative values = Better binding energy

Conclusion: Selected compounds

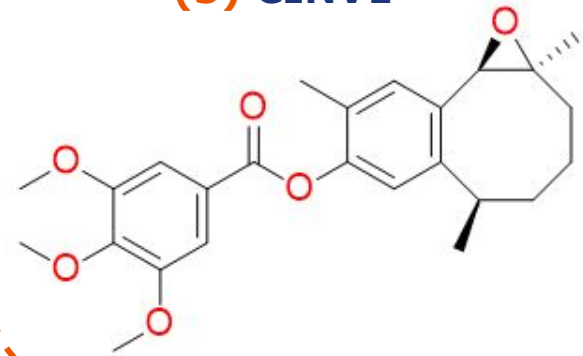


(1) FQNP278

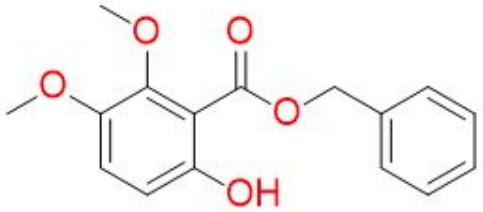


(2) FQNP280

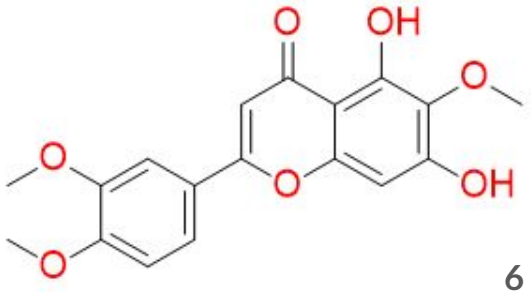
(5) CINV1



(4) FQNP443



(3) FQNP112



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