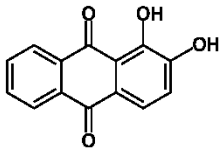
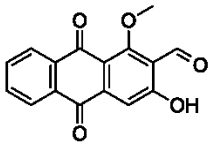
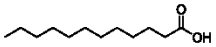
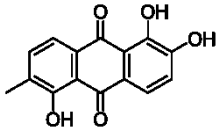
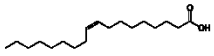
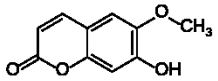
Cite this document as:
Patil, P., Shah, N. In silico pharmacokinetic analysis of Morinda citrifolia phytochemicals and their potential antagonistic effect on prostatic carcinoma proteins. DYSONA - Life Science, 2022;3(2):83-96. doi: 10.30493/dls.2022.351879

Supplementary Table 1. General properties of the investigated *Morinda citrifolia* phytochemicals

Ligand	Canonical Smiles	Molecular weight (g/mol)	Chemical structure
Alizarin	C1=CC=C2C(=C1)C(=O)C3=C(C2=O)C(=C(C=C3)O)O	240.21	
Damnacanthal	COC1=C2C(=CC(=C1C=O)O)C(=O)C3=CC=CC=C3C2=O	282.25	
Lauric acid	CCCCCCCCCCCC(=O)O	200.32	
Morindone	CC1=C(C2=C(C=C1)C(=O)C3=C(C2=O)C=CC(=C3O)O)O	270.24	
Oleic acid	CCCCCCCCC=CCCCCCCCC(=O)O	282.5	
Scopoletin	COC1=C(C=C2C(=C1)C=CC(=O)O2)O	192.17	

Supplementary Table 2. Physicochemical properties the investigated Morinda citrifolia phytochemicals

Ligand	NHA	Fraction CsP3	NRB	NHBA	NHBD	MR	TPSA (Å^2)
Alizarin	18	0	0	4	2	63.8	74.6
Damnacanthal	21	0.06	2	5	1	73.65	80.67
Lauric acid	14	0.92	10	2	1	61.57	37.3
Morindone	20	0.07	0	5	3	70.78	94.83
Oleic acid	20	0.83	15	2	1	89.94	37.3
Scopoletin	14	0.1	1	4	1	51	59.67

NHA: Number of heavy atoms
Fraction CsP3: The fraction of Csp3 hybridization
NRB: The number of rotatable bonds
NHBA: The number of hydrogen bond acceptors
NHBD: The number of hydrogen bond donors
MR: Molar refractivity
TPSA: Topological Polar Surface Area

Supplementary Table 3. Lipophilicity properties of the investigated Morinda citrifolia phytochemicals

Ligand	iLOGP	XLOGP3	WLOGP	MLOGP	SILICOS-IT	Consensus Log Po/w
Alizarin	1.85	3.16	1.87	0.67	2.55	2.02
Damnacanthal	1.19	2.5	1.99	0.27	3.25	1.84
Lauric acid	2.7	4.2	3.99	3.15	3.5	3.51
Morindone	2.09	3.27	1.89	0.36	2.55	2.03
Oleic acid	4.27	7.64	6.11	4.57	5.95	5.71
Scopoletin	1.86	1.53	1.51	0.76	1.94	1.52

Supplementary Table 4. Water solubility properties of the investigated *Morinda citrifolia* phytochemicals

Ligand	ESOL				ALI				SILICOS-IT			
	Log S	Solubility		Solubility class	Log S	Solubility		Solubility class	Log S	Solubility		Solubility class
		mg/ml	mol/l			mg/ml	mol/l			mg/ml	mol/l	
Alizarin	-3.18	3.69e-02	1.54e-04	Soluble	-4.40	9.63e-03	4.01e-05	Moderate	-4.10	1.91e-02	7.94e-05	Moderate
Damnacanthal	-3.46	9.88e-02	3.50e-04	Soluble	-3.84	4.08e-02	1.45e-04	Soluble	-4.74	5.12e-03	1.82e-05	Moderate
Lauric acid	-3.07	1.71e-01	8.55e-04	Soluble	-4.69	4.06e-03	2.03e-05	Moderate	-3.69	4.05e-02	2.02e-04	soluble
Morindone	-4.02	2.58e-02	9.56e-05	Moderate	-4.94	3.13e-03	1.16e-05	Moderate	-3.91	3.36e-02	1.24e-04	Soluble
Oleic acid	-5.41	1.09e-03	3.85e-06	Moderate	-8.26	1.54e-06	5.46e-09	Poor	-5.39	1.14e-03	4.04e-06	Moderate
Scopoletin	-2.46	6.70e-01	3.48e-03	Soluble	-2.39	7.79e-01	4.06e-03	Soluble	-3.17	1.31e-01	6.81e-04	Soluble

Supplementary Table 5. Pharmacokinetic properties of the investigated *Morinda citrifolia* phytochemicals

Ligand	GI absorption	BBB permeant	P-gp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	Log Kp (cm/s)
Alizarin	High	Yes	No	Yes	No	No	No	Yes	-5.52
Damnacanthal	High	No	No	Yes	No	No	No	Yes	-6.25
Lauric acid	High	Yes	No	No	No	No	No	No	-4.54
Morindone	High	No	No	Yes	No	No	No	Yes	-5.63
Oleic acid	High	No	No	Yes	No	Yes	No	No	-2.6
Scopoletin	High	Yes	No	Yes	No	No	No	No	-6.39

GI: Gastrointestinal
BBB: Blood-brain barrier
P-gp substrate
P-glycoprotein substrate
CYP: Cytochrome P450

Supplementary Table 6. Drug-likeness and bioavailability score properties of the investigated *Morinda citrifolia* phytochemicals

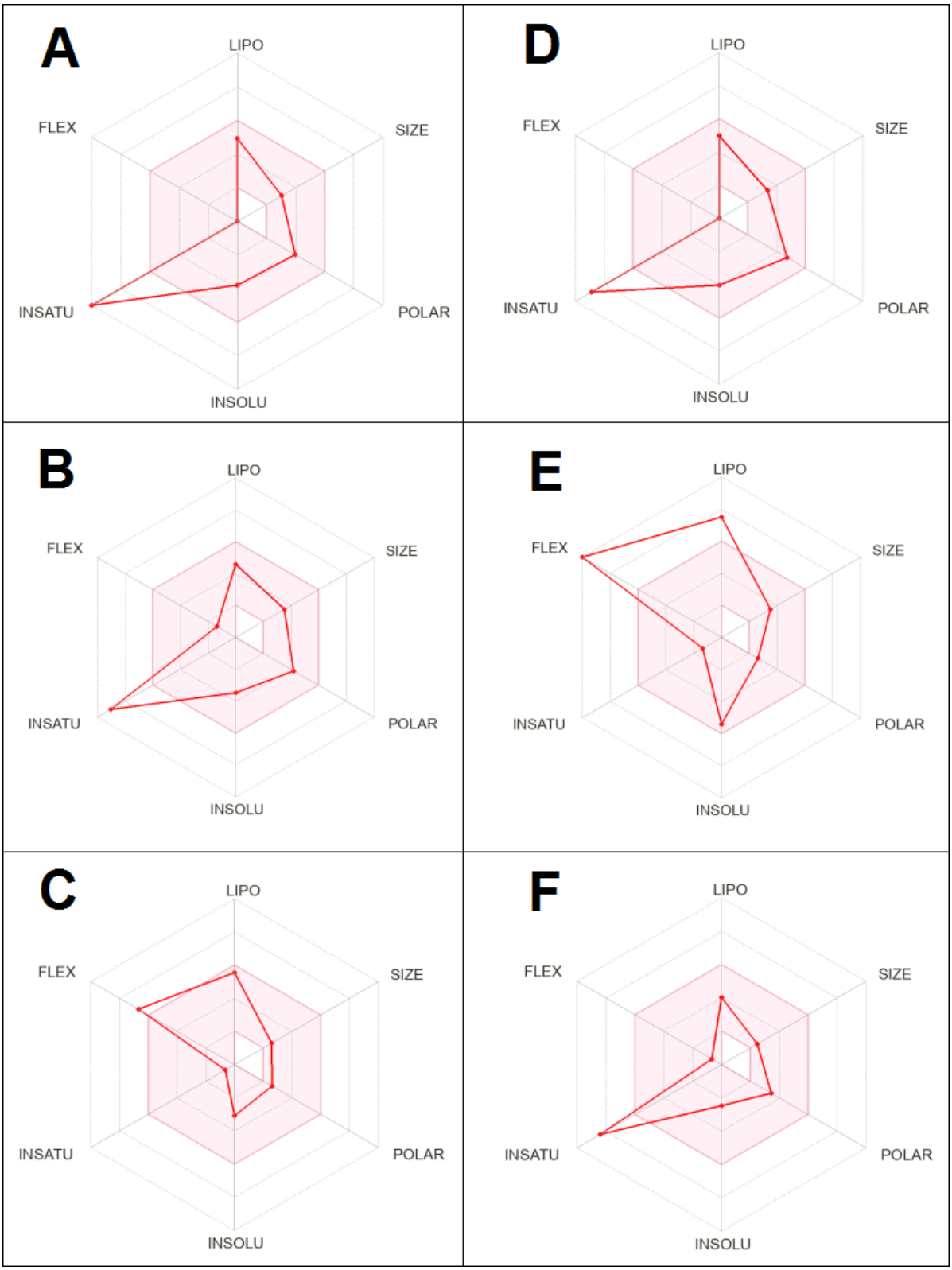
Ligand	Lipinski	Ghose	Veber	Egan	Muegge	Bioavailability score
Alizarin	Yes	Yes	Yes	Yes	Yes	0.55
Damnacanthal	Yes	Yes	Yes	Yes	Yes	0.55
Lauric acid	Yes	Yes	Yes	Yes	Yes	0.85
Morindone	Yes	Yes	Yes	Yes	Yes	0.55
Oleic acid	No; 1 violation: MLOGP>4.15	No; 1 violation: WLOGP>5.6	No; 1 violation: Rotors>10	No; 1 violation: WLOGP>5.88	No; 1 violation: XLOGP3>5	0.85
Scopoletin	Yes	Yes	Yes	Yes	No; 1 Violation: MW<200	0.55

Drug-likeness rule: Qualitative analysis defined by estimation ranges from specific physicochemical properties that make a molecule a possible oral drug. Drug-like Filters: Range based on computed/ predicted properties derived from known oral drugs [43].

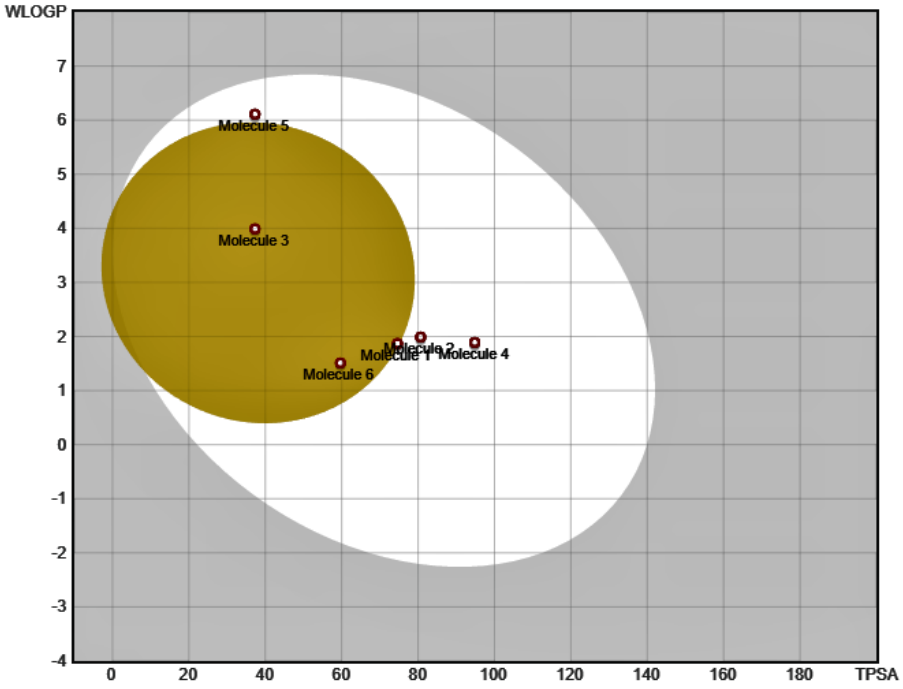
1. Lipinski filter (Ro5) – MW < 500, CLOGP < 5 (MLOGP (lipophilicity) < 4.15)[2], #Hydrogen bond donors less than or equal to 5 , # Hydrogen bond acceptors less than or equal 10 (not more than 1 criteria failing).
2. Ghose filter: 160 ≤ mol wt. ≤ 480, -0.4 ≤ WLOGP (lipophilicity) ≤5.6, 40 ≤ MR ≤ 130, and 20 ≤ Number of atoms ≤ 70,
3. Veber's filter: nRTB ≤ 10 and TPSA ≤ 131,
4. Egan filter (Pharmacia) predicts drug absorption based on the physical process involved in a membrane-permeant molecule: WLOGP (lipophilicity) ≤ 5.88, TPSA ≤ 132 Å[2],
5. Muegge filter: 200 ≤ mol wt. ≤ 600, -2 ≤ XLOGP3 (lipophilicity) ≤ 5, TPSA ≤ 150, Number of rings ≤ 7, Number of C > 4, Number of heteroatom. > 1, Number of rotatable bonds ≤ 15, H-bond acceptor (HBA) ≤ 10, and H-bond donors (HBD) ≤ 5

Supplementary Table 7. Medicinal chemistry properties of of the investigated *Morinda citrifolia* phytochemicals

Ligand	PAINS	Brenk	Lead-likeness	Synthetic accessibility
Alizarin	2 alerts: catechol_A, quinone_A	1 alert: catechol	No; 1 violation: MW<250	2.35
Damnacanthal	1 alert: quinone_A	1 alert: aldehyde	Yes	2.63
Lauric acid	0 alert	0 alert	No; 3 violations: MW<250, Rotors>7, XLOGP3>3.5	1.87
Morindone	2 alerts: catechol_A, quinone_A	1 alert: catechol	Yes	2.53
Oleic acid	0 alert	1 alert: isolated_alkene	No; 2 violations: Rotors>7, XLOGP3>3.5	3.07
Scopoletin	0 alert	1 alert: cumarine	No; 1 violation: MW<250	2.62



Supplementary Figure 1. Bioavailability radar for the investigated *Morinda citrifolia* phytochemicals. Alizarin (A), Damnacanthal (B), Lauric acid (C), Morindone (D), Oleic acid (E), Scopoletin (F). LIPO: lipophilicity, POLAR: polarity, INSOLU: insolubility, INSATU, insaturation, FLEX, flexibility. The pink area represents good oral bioavailability of the investigated molecule.



Supplementary Figure 2. Boiled egg visualization for the investigated *Morinda citrifolia* phytochemicals. Molecules 1 to 6 are alizarin, damnacanthal, lauric acid, morindone, oleic acid, and scopoletin in order. The yellow area contains molecules with high brain access, while the white contains molecules with high gastrointestinal absorption.