

Supplementary file

Screening of Phytochemical, Antimicrobial, and Antioxidant Properties of *Juncus acutus* from Northeastern Morocco

Yousra Hammouti ¹, Amine Elbouzidi ¹, Mohamed Taibi ^{1,2}, Reda Bellaouchi ³, El Hassania Loukili ², Mohamed Bouhrim ^{4,5}, Omar M. Noman ⁶, Ramzi A. Mothana ⁶, Mansour N. Ibrahim ⁷, Abdeslam Asehrou ³, Bouchra El Guerrouj ^{1,2}, and Mohamed Addi ^{1,*}

¹ Laboratoire d'Amélioration des Productions Agricoles, Biotechnologie et Environnement (LAPABE), Faculté des Sciences, Université Mohammed Premier, Oujda 60000, Morocco

² Centre de l'Oriental des Sciences et Technologies de l'Eau et de l'Environnement (COSTEE), Université Mohammed Premier, Oujda 60000, Morocco

³ Laboratory of Bioresources, Biotechnology, Ethnopharmacology and Health, Faculty of Sciences, Mohammed First University, Boulevard Mohamed VI, B.P. 717, Oujda 60000, Morocco

⁴ Laboratories TBC, Laboratory of Pharmacology, Pharmacokinetics and Clinical Pharmacy, Faculty of Pharmacy, University of Lille, 59000 Lille, France

⁵ Laboratory of Biological Engineering, Team of Functional and Pathological Biology, Faculty of Sciences and Technology, University Sultan Moulay Slimane, Beni Mellal 23000, Morocco

⁶ Department of Pharmacognosy, College of Pharmacy, King Saud University, Riyadh 11451, Saudi Arabia

⁷ Department of Agricultural Engineering, College of Food and Agriculture Sciences, King Saud University, Riyadh 11451, Saudi Arabia

* Correspondence: m.addi@ump.ac.ma

Table S1. Physiochemical and drug-likeness analysis of the major compounds found in *J. acutus* Leaves extract (JALE), and *J. acutus* roots extract (JARE). (1) Gallic acid, (2) Caffeic acid, (3) Ferulic acid, (4) Catechin, (5) Syringic acid, (6) Catechin hydrate, (7) 4-Hydroxybenzoic acid, (8) Naringin, (9) Cinnamic acid, (10) p-coumaric acid, (11) Sinapic acid, (12) Rutin hydrate, (13) Succinic acid, (14) Quercetin 3-O- β -D-glucoside, (15) Rutin, (16) Quercetin, (17) Kaempferol.

N°	Presence		HBD	HBA	TPSA (Å²)	Log Po/w (WLOGP)	Log S (SILICO S-IT)	Lipinski's Rule of Five	Veber filter
	JALE	JARE							
1	+	+	4	5	97.99	0.50	-0.20 (+++)	Yes; 0 violation	Yes; 0 violation
2	+	-	3	4	77.76	1.09	0.75 (+++)	Yes; 0 violation	Yes; 0 violation
3	++	-	2	4	66.76	1.39	1.26 (+++)	Yes; 0 violation	Yes; 0 violation
4	+	-	5	6	110.38	1.22	-2.14 (+++)	Yes; 0 violation	Yes; 0 violation
5	+	+	2	3	57.53	1.09	-1.17 (+++)	Yes; 0 violation	Yes; 0 violation
6	+	+	6	7	119.61	1.16	0.98 (+++)	Yes; 1 violation: NHorOH>5	Yes; 0 violation
7	+	+	2	3	57.53	1.09	-1.17 (+++)	Yes; 0 violation	Yes; 0 violation
8	+	+	8	14	225.06	-1.49	-0.49 (+++)	No; 3 violations: MW>500, NorO>10, NHorOH>5	No; 1 violation: TPSA> 140
9	+	+	1	2	37.30	1.68	1.70 (+++)	Yes; 0 violation	Yes; 0 violation
10	+	+	2	3	57.53	1.38	1.22 (+++)	Yes; 0 violation	Yes; 0 violation
11	-	+	2	5	75.99	1.40	1.33 (+++)	Yes; 0 violation	Yes; 0 violation
12	+	+	11	17	278.66	-1.75	-2.11 (+++)	No; 3 violations: MW>500, NorO>10, NHorOH>5	No; 1 violation: TPSA>140
13	-	+	2	4	74.60	-0.06	0.61 (+++)	Yes; 0 violation	Yes; 0 violation
14	-	+	8	12	210.51	-0.54	-0.59 (+++)	No; 2 violations: NorO>10, NHorOH>5	No; 1 violation: TPSA>140
15	+	+	10	16	269.43	-1.69	-2.11 (+++)	No; 3 violations: MW>500, NorO>10, NHorOH>5	No; 1 violation: TPSA>140
16	-	+	5	7	131.36	1.99	-3.24 (+++)	Yes; 0 violation	Yes; 0 violation
17	-	+	4	6	111.13	2.28	2.03 (+++)	Yes; 0 violation	Yes; 0 violation

HBD: Donors of Hydrogen Bonds; HBA: Acceptors of Hydrogen Bonds; Log Po/w: Partition Coefficient P; Log S: Solubility; (+++) High Solubility+; present; -absent

Table S2. The (ADME) pharmacokinetic characteristics of the identified compounds present JALE, and JARE. (1) Gallic acid, (2) Caffeic acid, (3) Ferulic acid, (4) Catechin, (5) Syringic acid, (6) Catechin hydrate, (7) 4-Hydroxybenzoic acid, (8) Naringin, (9) Cinnamic acid, (10) p-coumaric acid, (11) Sinapic acid, (12) Rutin hydrate, (13) Succinic acid, (14) Quercetin 3-O- β -D-glucoside, (15) Rutin, (16) Quercetin, (17) Kaempferol.

Prediction	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
ADME Prediction																	
Absorption Parameters																	
Bioavailability score	0.56	0.56	0.85	0.55	0.85	0.55	0.85	0.17	0.85	0.85	0.56	0.17	0.85	0.85	0.17	0.55	0.55
Caco-2 Permeability	-0.081	0.634	1.151	-0.283	0.176	0.159	1.151	-0.658	1.717	1.158	0.136	-1.248	0.603	0.242	-0.949	-0.229	0.032
Intestinal Absorption (%)	43.37	69.40	83.96	68.82	93.68	63.91	83.96	25.79	94.83	91.11	93.89	25.74	71.74	47.99	23.44	77.20	74.29
Distribution Parameters																	
Log K_p (cm/s)	-2.735	-2.722	-2.723	-2.735	-2.72	-2.735	-2.723	-2.735	-2.695	-2.323	-2.72	-2.735	-2.735	-2.735	-2.735	-2.735	-2.735
VDss	-1.855	-1.098	-1.557	1.027	-1.367	1.023	-1.557	0.619	-1.051	-0.406	-0.797	0.576	-1.013	1.846	1.663	1.559	1.274
BBB Permeability	-1.102	-0.647	-0.334	-1.054	-0.239	-1.06	-0.334	-1.600	0.446	-0.257	-0.198	-2.187	-0.163	-1.688	-1.899	-1.098	-0.939
Metabolism Parameters																	
CYP2D6, and CYP3A4 Substrate	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
CYP2D6, and CYP3A4 Inhibitors	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
Excretion Parameters																	
Total Clearance	0.518	0.508	0.593	0.183	0.623	0.181	0.593	0.318	0.781	0.672	0.741	-0.081	0.722	0.394	-0.369	0.407	0.477
Renal OCT2 Substrate	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No

BBB: blood-brain barrier; Log BB > 0.3, molecule BBB permeant, Log BB < -1 molecule poorly distributed across the BBB.

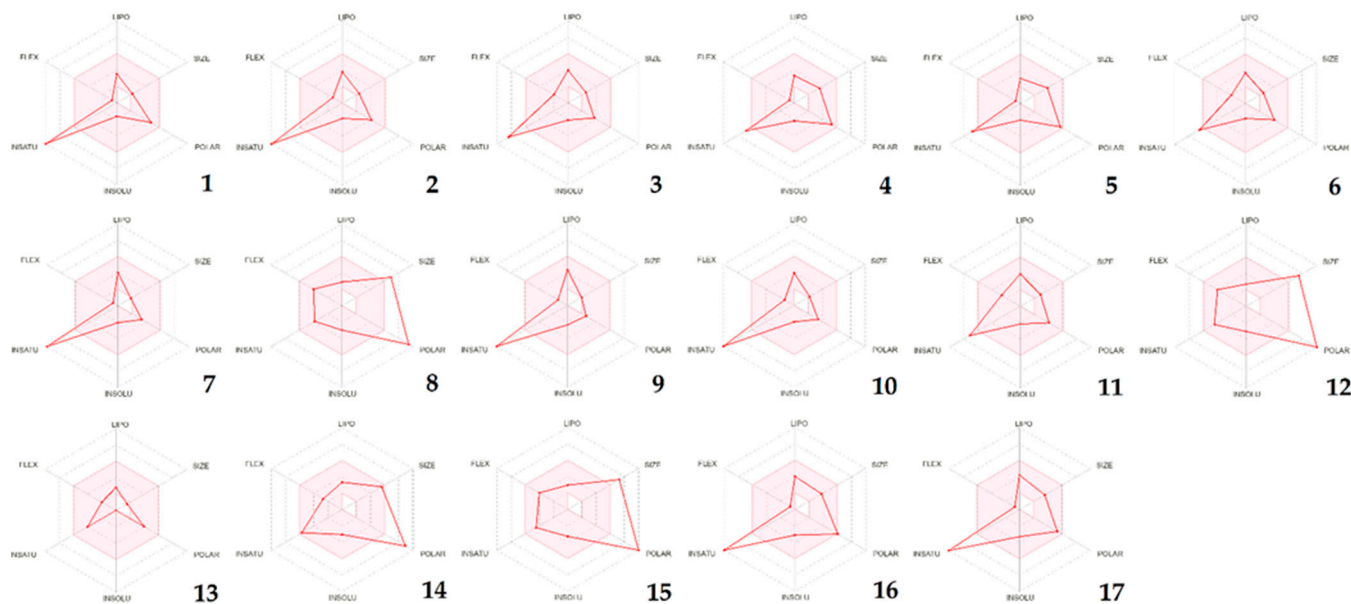


Figure S1. JALE, and JARE compounds' bioavailability radars based on six physicochemical properties (lipophilicity, size, polarity, solubility, flexibility, and saturation). Note: (1) Gallic acid, (2) Caffeic acid, (3), Ferulic acid (4), Catechin, (5) Syringic acid, (6) Catechin hydrate, (7) 4-Hydroxybenzoic acid, (8) Naringin, (9) Cinnamic acid, (10) p-coumaric acid, (11) Sinapic acid, (12) Rutin hydrate, (13) Succinic acid, (14) Quercetin 3-O- β -D-glucoside, (15) Rutin, (16) Quercetin, (17) Kaempferol.

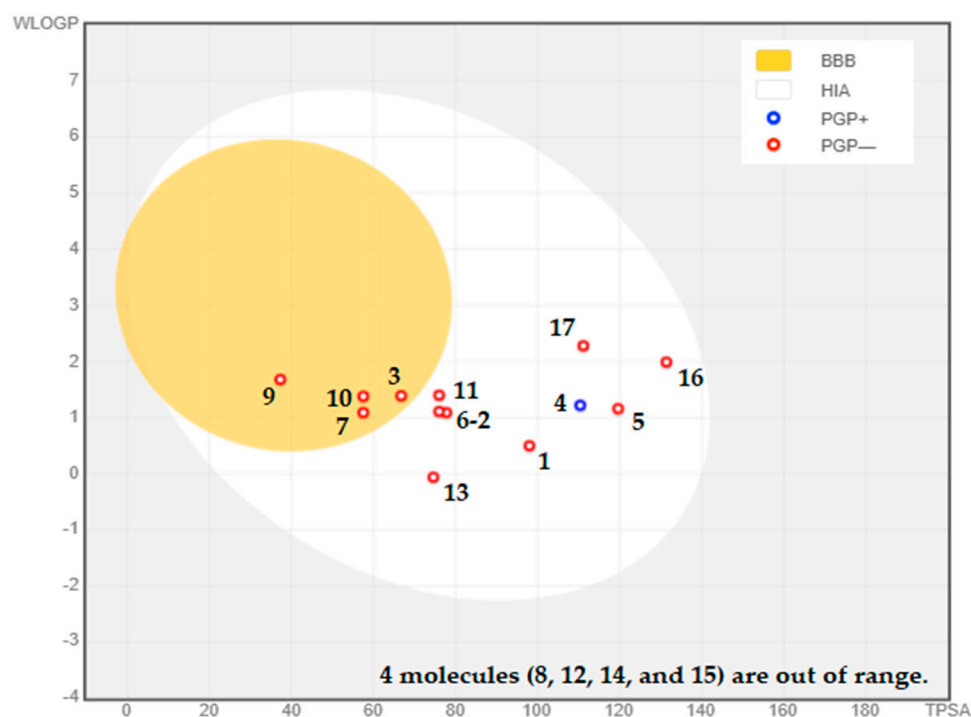


Figure S2. The BOILED-EGG Framework: Employed for Evaluating JALE, and JARE Composition Regarding Blood-Brain Barrier Permeability, Gastrointestinal Absorption, and Interaction with P-glycoprotein as Substrates or Inhibitors. (1) Gallic acid, (2) Caffeic acid, (3), Ferulic acid (4), Catechin, (5) Syringic acid, (6) Catechin hydrate, (7) 4-Hydroxybenzoic acid, (8) Naringin, (9) Cinnamic acid, (10) p-coumaric acid, (11) Sinapic acid, (12) Rutin hydrate, (13) Succinic acid, (14) Quercetin 3-O- β -D-glucoside, (15) Rutin, (16) Quercetin, (17) Kaempferol.

Table S3. Prediction of toxicity, and the toxic endpoints of the major compounds found in JALE, and JARE. (1) Gallic acid, (2) Caffeic acid, (3) Ferulic acid, (4) Catechin, (5) Syringic acid, (6) Catechin hydrate, (7) 4-Hydroxybenzoic acid, (8) Naringin, (9) Cinnamic acid, (10) p-coumaric acid, (11) Sinapic acid, (12) Rutin hydrate, (13) Succinic acid, (14) Quercetin 3-O- β -D-glucoside, (15) Rutin, (16) Quercetin, (17) Kaempferol.

N	Predicted LD ₅₀ (mg/kg)	Class	Hepatotoxicity		Cytotoxicity		Immunotoxicity		Mutagenicity		Carcinogenicity	
			Predi.	Prob.	Predi.	Prob.	Predi.	Prob.	Predi.	Prob.	Predi.	Prob.
1	2000	IV	Ina.	0.94	Ina.	0.91	Ina.	0.99	Ina.	0.61	Act.	0.56
2	2980	V	Ina.	0.98	Ina.	0.86	Ina.	0.50	Ina.	0.57	Act.	0.78
3	1772	IV	Ina.	0.96	Ina.	0.88	Act.	0.91	Ina.	0.51	Ina.	0.61
4	10000	VI	Ina.	0.55	Ina.	0.84	Ina.	0.96	Ina.	0.72	Ina.	0.51
5	10000	VI	Act.	0.55	Ina.	0.84	Ina.	0.97	Ina.	0.73	Ina.	0.76
6	1700	IV	Ina.	0.93	Ina.	0.97	Ina.	0.97	Ina.	0.58	Ina.	0.70
7	2200	V	Ina.	0.99	Ina.	0.86	Ina.	0.99	Ina.	0.52	Ina.	0.51
8	2300	V	Ina.	0.73	Ina.	0.66	Act.	0.99	Ina.	0.81	Ina.	0.90
9	2500	V	Ina.	0.96	Ina.	0.83	Ina.	0.95	Act.	0.54	Ina.	0.82
10	1048	IV	Ina.	0.99	Ina.	0.98	Ina.	0.78	Ina.	0.68	Ina.	0.64
11	1772	IV	Ina.	0.87	Ina.	0.96	Act.	0.89	Ina.	0.54	Ina.	0.67
12	2850	V	Ina.	0.92	Ina.	0.81	Ina.	0.86	Act.	0.53	Act.	0.51
13	2260	V	Ina.	0.98	Ina.	0.75	Ina.	0.99	Ina.	0.83	Ina.	0.80
14	1034	IV	Ina.	0.98	Ina.	0.86	Ina.	0.99	Act.	0.51	Ina.	0.67
15	5000	V	Ina.	0.88	Ina.	0.64	Act.	0.98	Ina.	0.80	Ina.	0.91
16	159	III	Ina.	0.51	Ina.	0.99	Ina.	0.87	Ina.	0.69	Act.	0.68
17	3919	V	Ina.	0.52	Ina.	0.98	Ina.	0.96	Ina.	0.68	Ina.	0.72