

Supplement to Exploring the Role of Sodium-Glucose Cotransporter as a New Target for Cancer Therapy. J Pharm Pharm Sci (www.cspsCanada.org) 25, 253 - 265, 2022

Table 1S. Primers' forward and reverse sequences of each gene. SGLT2: gene for Sodium-glucose cotransporter 2; Bcl-2: gene for B-cell lymphoma 2; VEGF: gene for Vascular endothelial growth factor; GAPDH: gene for Glyceraldehyde 3-phosphate dehydrogenase.

Primer	Primer sequences
SGLT2	forward: 5-GATTACACGGTGACAGGAGGG-3 reverse: 5-CGGAGCAGGTGGTAGGAGT-3
Bcl-2	forward: 5-TTGTGGCCTTCTTTGAGTTCGGTG -3 reverse: 5- GGTGCCGGTTCAGGTACTCAGTCA-3
VEGF	forward: 5-CTACCTCCACCATGCCAAGT-3 reverse: 5-GCAGTAGCTGCGCTGATAGA-3
GAPDH	forward: 5-ACAACCTTGGTATCGTGGAAGG-3 reverse: 5-GCCATCACGCCACAGTTTC-3

Table 2S. The 50% inhibitory concentration (IC₅₀) and fold changes values of combined canagliflozin, ipragliflozin and chemotherapeutic agents in different cell lines for 48 h at 1:5 and 1:10

A-549 cell line					
		1:5 ratio		1:10 ratio	
Cisplatin: Canagliflozin	IC ₅₀ in ratio	72.9	241	53.7	325.6
	Fold increase	1.6	3.4	1.2	4.6
Cisplatin: Ipragliflozin	IC ₅₀ in ratio	51.8	259.1	48.3	483.7
	Fold increase	1.1	1.2	1	2.3
Raloxifene: Canagliflozin	IC ₅₀ in ratio	18.5	55.4	6.4	64.3
	Fold reduction	2.2	1.2	6.3	1
Raloxifene: Ipragliflozin	IC ₅₀ in ratio	26.5	131.4	12.9	129.9
	Fold reduction	1.5	1.5	3.1	1.5
Caco-2 cell line					
		1:5 ratio		1:10 ratio	
Doxorubicin: Canagliflozin	IC ₅₀ in ratio	3	11.2	1.7	11.2
	Fold reduction	2.9	4.3	5.1	4.3
Doxorubicin: Ipragliflozin	IC ₅₀ in ratio	8.1	30.6	6.3	22.1
	Fold reduction	1.1	5.5	1.4	7.4
MCF-7 cell line					
		1:5 ratio		1:10 ratio	
Doxorubicin: Canagliflozin	IC ₅₀ in ratio	2.1	11.6	3.5	24
	Fold reduction	4.1	3.5	2.5	1.7
Doxorubicin: Ipragliflozin	IC ₅₀ in ratio	3.5	18.3	3.6	27.6
	Fold reduction	2.5	3.4	2.4	2.3
Raloxifene: Canagliflozin	IC ₅₀ in ratio	4.5	19.7	2.4	23.2
	Fold reduction	6.6	2.1	12.5	1.8
Raloxifene: Ipragliflozin	IC ₅₀ in ratio	13	57.3	5.4	35.4
	Fold reduction	2.3	1.1	5.6	1.7
Du-145 cell line					
		1:5 ratio		1:10 ratio	
Cisplatin: Canagliflozin	IC ₅₀ in ratio	12	58.4	6.7	65.5
	Fold increase	2	1.3	1.1	1.4
Cisplatin: Ipragliflozin	IC ₅₀ in ratio	35.5	175.6	18.8	185.9
	Fold increase	6.1	1.1	3.2	1.1
Pnac-1 cell line					
		1:5 ratio		1:10 ratio	
Cisplatin: Canagliflozin	IC ₅₀ in ratio	43.6	218.5	62.8	654.5
	Fold increase	1.3	4.7	1.8	14.2
Cisplatin: Ipragliflozin	IC ₅₀ in ratio	63.3	322.7	33.5	335.7
	Fold increase	1.8	1.2	1.0	1.3

Table 3S. Combination index (CI) values for combined treatment of SGLT2 inhibitors and other chemotherapeutic agents against different cell lines for 48h at different ratios.

A-549 cell line				
	Cisplatin: Canagliflozin		Cisplatin: Ipragliflozin	
Combination ratio	1:5	1:10	1:5	1:10
Combination index	1.9	1.8	1.5	1.3
	Raloxifene: Canagliflozin		Raloxifene: Ipragliflozin	
Combination ratio	1:5	1:10	1:5	1:10
Combination index	0.73	0.89	0.89	0.92
MCF-7 cell line				
	Raloxifene: Canagliflozin		Raloxifene: Ipragliflozin	
Combination ratio	1:5	1:10	1:5	1:10
Combination index	0.34	0.19	0.68	0.32
	Doxorubicin: Canagliflozin		Doxorubicin: Ipragliflozin	
Combination ratio	1:5	1:10	1:5	1:10
Combination index	0.35	0.74	0.87	0.44
Caco-2 cell line				
	Doxorubicin: Canagliflozin		Doxorubicin: Ipragliflozin	
Combination ratio	1:5	1:10	1:5	1:10
Combination index	0.44	0.82	0.59	0.27
Du-145 cell line				
	Cisplatin: Canagliflozin		Cisplatin: Ipragliflozin	
Combination ratio	1:5	1:10	1:5	1:10
Combination index	1.9	2.8	1.5	4.5
Panc-1 cell line				
	Cisplatin: Canagliflozin		Cisplatin: Ipragliflozin	
Combination ratio	1:5	1:10	1:5	1:10
Combination index	2.5	1.4	2	3.2