

Supplementary Table 1: A 24-hour growth inhibition comparison of linagliptin, rivaroxaban, cisplatin, and a mixture.

Concentration (µg/ml)	Growth inhibition (mean ± SE ^a)				^b LSD value
	linagliptin	Rivaroxaban	mix	Cisplatin	
0.1	D 1.00 ± 1.000	D 5.00 ± 3.000	D 4.00 ± 3.000	D 0.00 ± 0.000	N. S
1	CD 8.00 ± 3.000 ab	CD 9.00 ± 2.000 a	CD 12.00 ± 3.000 a	D 1.00 ± 1.000 b	7.98
10	BC 17.00 ± 2.000	BC 18.00 ± 3.000	C 18.00 ± 4.000	C 8.00 ± 3.000	N. S
100	AB 20.00 ± 5.000 b	A 29.00 ± 1.000 a	B 33.00 ± 3.000 a	B 31.00 ± 1.000 a	11.3
1000	A 30.33 ± 3.055 b	AB 26.00 ± 4.000 c	A 57.00 ± 2.000 a	A 39.00 ± 1.000 b	10.37
^b LSD value	11.32	10.16	10.54	5.64	-
IC 50	1861.5 µg/ml	2024.8 µg/ml	805.3 µg/ml	1280.8 µg/ml	-
a: standard error, b: least significant difference. Capital letters within the same column indicate statistically significant differences, while variations in lowercase letters within the same rows also signify statistically significant differences.: significant at (P<0.05)					

Supplementary Table 2: A 72-hour growth inhibition comparison of linagliptin, Rivaroxaban , cisplatin, and a mixture.

Concentration (µg/ml)	Growth inhibition (mean ± SE ^a)				^b LSD value
	linagliptin	Rivaroxaban	mix	cisplatin	
0.1	C 12.00 ± 2.000 ab	C 17.00 ± 1.000 a	D 10.00 ± 2.000 bc	D 4.00 ± 2.000 c	6.78
1	BC 23.00 ± 3.000 a	BC 22.00 ± 2.000 a	CD 18.00 ± 3.000 ab	CD 10.00 ± 2.000 b	9.6
10	AB 33.00 ± 4.000 a	B 32.00 ± 2.000 a	BC 27.00 ± 4.000 ab	C 17.00 ± 1.000 b	11.9
100	A 37.00 ± 1.000 a	AB 44.00 ± 4.000 a	B 36.00 ± 2.000 a	B 36.00 ± 2.000 a	N. S
1000	A 44.00 ± 4.000 bc	A 39.00 ± 5.000 c	A 70.00 ± 3.000 a	A 52.00 ± 3.000 b	10.82
^b LSD value	11.04	11.5	10.14	7.28	-
IC 50	1252.6 µg/ml	1239.7 µg/ml	579 µg/ml	904.7 µg/ml	-
a: standard error, b: least significant difference. Capital letters within the same column indicate statistically significant differences, while variations in lowercase letters within the same rows also signify statistically significant differences.: significant at (P<0.05)					

Supplementary Table 3: Comparison of the docking scores of each mixture ingredient with its corresponding standard medicine.

Molecular target	Linagliptin	Ralimetinib	Rivaroxaban	Sotorasib
Mutant P38 MAPK kinase	-7.9	-8.7	-	-
RAS kinase	-	-	-8.7	-6.2

Supplementary Table 4: CI and DRI for the linagliptin- rivaroxaban mixture cytotoxicity at 24 hrs. incubation periods

concentration µg/ml			Con. ratio	CI value	Combination behaviour	DRI value	
linagliptin	rivaroxaban	Mix	1:1			linagliptin	rivaroxaban
0.05	0.05	0.1		41.8756	Very Strong Antagonism	13.2989 *	0.02392
0.5	0.5	1		0.09818	Very Strong Synergism	32.3770 *	14.8604 *
5	5	10		0.10589	Strong Synergism	11.6667 *	49.5655 *
50	50	100		0.09780	Very Strong Synergism	10.2797 *	1908.82*
500	500	1000		0.06766	Very Strong Synergism	14.7804 *	280688 *

The CI (Combination Index) and DRI (Dose Reduction Index) Values were evaluated utilizing Compusyn software. A CI number exceeding 1 indicates antagonism, a CI value of 1 denotes an additive effect, and a CI value below 1 suggests synergism. A dose reduction index (DRI) exceeding one correlates with reduced toxicity. * indicates a favourable decline in the effective cytotoxic concentration [56] .

Supplementary Table 5: CI and DRI for the linagliptin- rivaroxaban mixture cytotoxicity at 72 hrs. incubation periods

concentration µg/ml			Con. ratio	CI value	Combination behaviour	DRI value	
linagliptin	rivaroxaban	Mix	1:1			linagliptin	rivaroxaban
0.05 µg/ml	0.05 µg/ml	0.1		3.482E8	Strong Antagonism	0.19225	E-92.87
0.5 µg/ml	0.5 µg/ml	1		788.072	Very Strong Antagonism	0.81901	0.00127
5 µg/ml	5 µg/ml	10		0.75250	Moderate Synergism	1.45158*	15.7242*
50 µg/ml	50 µg/ml	100		0.68368	Synergism	1.46279*	19448.0*
500 µg/ml	500 µg/ml	1000		0.00269	Very Strong Synergism	371.359*	1.50E17*

The CI (Combination Index) and DRI (Dose Reduction Index) Values were evaluated using Compusyn software. A CI number exceeding 1 indicates antagonism, a CI value of 1 denotes an additive effect, and a CI value below 1 suggests synergism. A dose reduction index (DRI) exceeding one correlates with reduced toxicity, * indicates a favourable decline in the effective cytotoxic concentration [56]