第二節 藥理活性試驗結果

壹、抗血小板凝集活性試驗

將前述合成出及經結構判定正確之化合物21-33、41-48、50-53、61-68、70-73、81-93、101-109、111-114、116-118及120-123藉著：

(1)thrombin (0.1 unit/ml)、AA (100 μM)、collagen (10 μg/ml)及PAF (2 ng/ml)為血小板凝集誘導劑 (inducer)，以兔子血小板進行抗血小板凝集活性之篩選試驗，篩選結果如Table 1至Table 3所示。

(2)thrombin (0.1 unit/ml)、AA (200 μM)及collagen (10 μg/ml)為血小板凝集誘導劑 (inducer)，以人類血小板進行抗血小板凝集活性之篩選試驗，篩選結果如Table 4至Table 6所示。

由測試的結果發現：

(一)對於thrombine所引起血小板凝集的抑制試驗

從化合物 21-28、30-33、41-48、50-53、61-68、70-73、81-93、101-109、111-114、116-118 及 120-123 (見 Table 1 至 Table 6)的凝集百分比看來，在濃度 100 μg/ml 時，化合物 27 及 30 分別呈現弱的抑制活性，但是發現化合物 32 呈現明顯的抑制活性，而其所接的取代基溴原子為拉電子基，因此減少官能基對於水相的親和力，導致分配係數增加，脂溶性增加[84]，所以藥物較容易到達作用位置與接受器結合產生藥效。其他化合物則無明顯的抑制活性。

綜合上述，發現 ethyl 5-(2'-alkoxycarbonyl substituted phenoxy)-furan-2-carboxylates (**21-33**)類衍生物的活性較明顯。在 ethyl 5-(2'-alkoxycarbonyl substituted phenoxy)furan-2-carboxylates (**21-33**)類衍生物中將溴原子導入苯環時，具有較高的活性，相較之下，若將氯原子導入苯環，則其活性降低，此外，若將甲基、甲氧基或碘原子導入苯環，則其活性降得更低。

(二)對於 AA 所引起血小板凝集的抑制試驗

從化合物 21-28、30-33、41-48、50-53、61-68、70-73、81-93、101-109、111-114、116-118 及 120-123 (見 Table 1 至 Table 6)的凝集百分比看來，化合物 25、27、28、32、92、93 及 123 分別呈現弱的抑制活性 (其 IC_{50} 值大約在 69-100 μM 之間)，但是發現化合物 61、62、64 及 72 呈現明顯的抑制活性，其 IC_{50} 值分別為 55.1 μM、55.5 μM、37.6 μM 及 55.4 μM。其他化合物則無明顯的抑制活性。

綜合上述，發現 substituted furo[2,3-*b*]chromone-2-carboxylic acid ethyl esters (**61-68 及 70-73**)類衍生物的活性較明顯。在 substituted

furo[2,3-*b*]chromone-2-carboxylic acid ethyl esters (**61-68 及 70-73**)類衍生物中將甲基或溴原子導入環上時，具有較高的活性，相較之下，若將碘原子導入環上，則其活性降低，此外，若將甲氧基或氯原子導入環上，則其活性降得更低。

(三)對於collagen所引起血小板凝集的抑制試驗

從化合物 **21-28**、**30-33**、**41-48**、**50-53**、**61-68**、**70-73**、**81-93**、**101-109**、**111-114**、**116-118** 及 **120-123** (見 Table 1 至 Table 6)的凝集百分比看來，在濃度 100 μg/ml 時，化合物 **21**、**23**、**33**、**61** 及 **62** 分別呈現弱的抑制活性，但是發現化合物 **22**、**24-28**、**30-32**、**68**、**72** 及 **73** 呈現明顯的抑制活性；另外，在濃度 100 μM 時，化合物 **91-93** 及 **123** 分別呈現弱的抑制活性。然而, 其他化合物則無明顯的抑制活性。

綜合上述，發現 ethyl 5-(2'-alkoxycarbonyl substituted phenoxy)-furan-2-carboxylates (**21-33**) 類及 substituted furo[2,3-*b*]chromone-2-carboxylic acid ethyl esters (**61-68** 及 **70-73**)類衍生物的活性較明顯。在 ethyl 5-(2'-alkoxycarbonyl substituted phenoxy)furan-2-carboxylates (**21-33**)類衍生物中將甲氧基、氯原子或溴原子導入苯環時, 具有較高的活性, 相較之下, 若將甲基導入苯環，則其活性降低，此外，若將碘原子導入苯環，則其活性降得更低。另外，在 substituted furo[2,3-*b*]chromone-2-carboxylic acid ethyl esters (**61-68** 及 **70-73**)類衍生物中將甲氧基、溴原子或碘原子導入環上時，具有較高的活性，相較之下，若將甲基導入環上，則其活性降低，此外，若將氯原子導入環上，則其活性降得更低。

(四)對於PAF所引起血小板凝集的抑制試驗

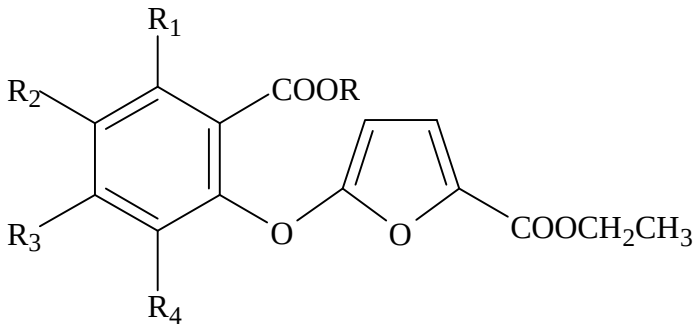
從化合物 **21-28**、**30-33**、**41-48**、**50-53**、**61-68** 及 **70-73** (見 Table 1 至 Table 6)的凝集百分比看來，在濃度 100 μg/ml 時，化合物 **21**、**22** 及 **26** 分別呈現弱的抑制活性，但是發現化合物 **24**、**25**、**27**、**28** 及 **30-32** 呈現明顯的抑制活性。其他化合物則無明顯的抑制活性。

綜合上述，發現 ethyl 5-(2'-alkoxycarbonyl substituted phenoxy)-furan-2-carboxylates (**21-33**)類衍生物的活性較明顯。在 ethyl 5-(2'-alkoxycarbonyl substituted phenoxy)furan-2-carboxylates (**21-33**)類衍生物中將甲基、甲氧基、氯原子或溴原子導入苯環時，具有較高的活性，相較之下，若將碘原子導入苯環，則其活性降得更低。

著者由 thrombine、AA、collagen 及 PAF 所引起血小板凝集的抑制試驗中發現，酯類化合物如 ethyl 5-(2'-alkoxycarbonyl substituted phenoxy)furan-2-carboxylates (**21-33**) 類及 substituted

furo[2,3-*b*]-chromone-2-carboxylic acid ethyl esters (**61-68及70-73**)**類衍生物比羧酸類化合物具有較明顯的抑制活性，其中化合物** ethyl 5-(2'-methoxy-carbonyl-4'-bromophenoxy)furan-2-carboxylate (**32**)**效果最好。**

Table 1. The inhibitory effect of ethyl 5-(2'-alkoxycarbonyl substituted phenoxy)-furan-2-carboxylates on rabbit platelet aggregation induced by thrombin, AA, collagen and PAF (*in vitro*)



21: R=CH_3, R_1=R_2=R_3=R_4=H
22: R=CH_3, R_1=R_2=R_3=H, R_4=CH_3
23: R=CH_3, R_1=R_2=R_4=H, R_3=CH_3
24: R=CH_3, R_1=R_3=R_4=H, R_2=CH_3
25: R=C_2H_5, R_2=R_3=R_4=H, R_1=CH_3
26: R=CH_3, R_1=R_2=R_3=H, R_4=OCH_3
27: R=CH_3, R_1=R_2=R_4=H, R_3=OCH_3
28: R=CH_3, R_1=R_3=R_4=H, R_2=OCH_3
30: R=CH_3, R_1=R_2=R_4=H, R_3=Cl
31: R=CH_3, R_1=R_3=R_4=H, R_2=Cl
32: R=CH_3, R_1=R_3=R_4=H, R_2=Br
33: R=CH_3, R_1=R_3=R_4=H, R_2=I

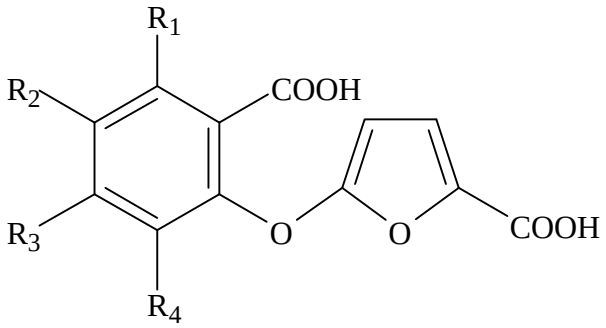
Compound	conc. (μg/ml)	Percent Aggregation: thrombin	AA	collagen	PAF
	Control	90.9±1.2(3)	89.5±1.0(4)	89.2±1.3(4)	91.7±0.5(4)
21	(100)	87.7±0.2*(3)	2.8±2.3***(3)	39.3±9.8***(4)	33.0±0.6***(3)
	(50)		78.4±1.0***(3)		
	(20)		83.2±1.6**(3)		
	IC_{50}		192.4 μM		
22	(100)	88.7±0.9(3)	0.0±0.0***(3)	5.4±2.8***(4)	39.6±9.7***(4)
	(50)		73.2±4.7**(3)		
	(20)		86.8±1.0(3)		
	IC_{50}		179.3 μM		
23	(100)	85.0±0.7**(3)	0.0±0.0***(3)	13.9±6.9***(4)	71.6±1.3***(3)
	(50)		72.5±2.4***(3)		
	(20)		87.0±1.1(3)		
	IC_{50}		179.0 μM		
24	(100)	78.8±2.3***(3)	0.0±0.0***(4)	9.7±5.5***(4)	0.0±0.0***(3)
	(50)		9.9±8.6***(4)		77.2±2.0***(3)
	(20)		83.7±3.2(4)		
	IC_{50}		128.1 μM		
	Control	92.3±0.3(3)	91.0±1.5(3)	89.5±0.6(4)	94.7±1.8(3)

25	(100)	75.2±1.3***(3)	0.0±0.0***(3)	0.0±0.0***(3)	0.0±0.0***(3)
	(50)		0.0±0.0***(3)	1.4±1.2***(3)	16.0±9.9***(3)
	(20)		84.3±0.2**(3)	84.0±1.2***(3)	86.5±0.5**(3)
	IC_{50}		85.7 μM	118.4 μM	131.7 μM
	Control	88.5±1.2(4)	87.2±0.5(5)	90.3±0.5(3)	89.4±0.3(4)
26	(100)	80.5±1.4***(3)	0.8±0.8***(5)	0.0±0.0***(3)	44.3±9.3***(4)
	(50)		37.2±9.6***(5)		
	(20)		56.6±10.4**(5)		
	(10)		81.5±2.5*(5)		
	IC_{50}		121.7 μM		
27	(100)	48.3±1.9***(3)	0.0±0.0***(5)	0.0±0.0***(3)	0.0±0.0***(3)
	(50)		16.9±11.0***(5)		45.3±3.9***(3)
	(20)		47.9±12.8**(5)		70.7±1.4***(3)
	(10)		68.1±7.2*(5)		78.7±0.9***(3)
	(5)		85.9±1.5(5)		
	IC_{50}		99.3 μM		136.5 μM
28	(100)	71.0±3.6***(3)	0.0±0.0***(5)	0.0±0.0***(3)	0.0±0.0***(3)
	(50)		4.8±4.3***(5)		64.5±1.3***(3)
	(20)		40.5±12.7**(5)		85.1±1.4**(3)
	(10)		83.0±1.9(5)		
	IC_{50}		93.9 μM		163.8 μM
30	(100)	44.3±10.8***(4)	0.0±0.0***(5)	0.0±0.0***(3)	0.0±0.0***(3)
	(50)		4.3±3.8***(5)		60.6±2.3***(3)
	(20)		64.1±5.8***(5)		84.9±1.2***(3)
	(10)		74.8±3.7**(5)		
	(5)		84.0±1.1*(5)		
	IC_{50}		101.5 μM		158.7 μM
31	(100)	68.0±7.2*(4)	0.0±0.0***(5)	0.0±0.0***(3)	0.0±0.0***(3)
	(50)		19.9±6.0***(5)		68.7±1.5***(3)
	(20)		69.6±5.0**(5)		85.5±2.3(3)
	(10)		83.4±1.6*(5)		
	IC_{50}		117.0 μM		164.6 μM
32	(100)	5.4±2.8***(3)	0.0±0.0***(3)	0.0±0.0***(3)	0.0±0.0***(4)
	(50)		0.0±0.0***(3)		51.6±6.2***(4)
	(20)		78.5±2.5***(3)		71.8±4.1***(4)
	(10)		85.2±0.9(3)		82.4±2.4*(4)
	IC_{50}		71.1 μM		124.9 μM
	Control	92.7±0.6(3)	88.2±0.3(4)	90.6±0.4(4)	91.1±0.9(4)

33	(100)	84.0±0.7***(3)	38.9±15.6**(4)	34.4±1.5***(3)	64.8±8.1**(4)
	(50)		57.5±16.8(4)		
	(20)		84.7±2.1(4)		
	IC_{50}		177.8 μM		
Aspirin	IC_{50}		20.0 μM		

Platelet were incubated with tested sample or 0.5% DMSO at 37 ℃ for 1min, then thrombin (0.1 U/ml), AA (100 μM), collagen (10 μg/ml) or PAF (2 ng/ml) was added to trigger the aggregation. Values are presented as mean±S.E. , N=3-5. *: P<0.05, **: P<0.01, ***: P<0.001.

Table 2. The inhibitory effect of 5-(2'-carboxyl substituted phenoxy)furan-2-carboxylic acids on rabbit platelet aggregation induced by thrombin, AA, collagen and PAF (*in vitro*)



41: $R_1=R_2=R_3=R_4=H$ **47**: $R_1=R_2=R_4=H$, $R_3=OCH_3$

42: $R_1=R_2=R_3=H$, $R_4=CH_3$ **48**: $R_1=R_3=R_4=H$, $R_2=OCH_3$

43: $R_1=R_2=R_4=H$, $R_3=CH_3$ **50**: $R_1=R_2=R_4=H$, $R_3=Cl$

44: $R_1=R_3=R_4=H$, $R_2=CH_3$ **51**: $R_1=R_3=R_4=H$, $R_2=Cl$

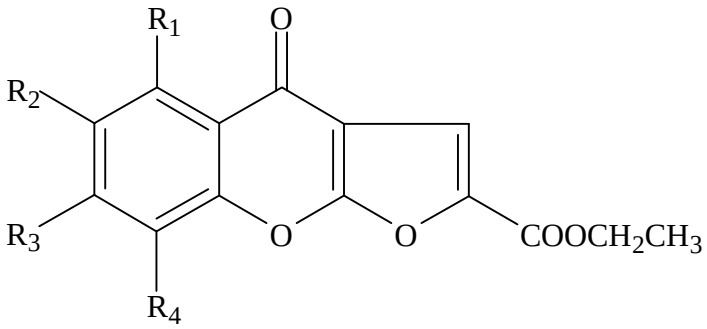
45: $R_2=R_3=R_4=H$, $R_1=CH_3$ **52**: $R_1=R_3=R_4=H$, $R_2=Br$

46: $R_1=R_2=R_3=H$, $R_4=OCH_3$ **53**: $R_1=R_3=R_4=H$, $R_2=I$

Compound	conc. (μg/ml)	Percent Aggregation			
		thrombin	AA	collagen	PAF
	Control	90.9±1.2(3)	89.5±1.0(4)	89.2±1.3(4)	91.7±0.5(4)
41	(100)	90.3±0.7(3)	87.0±1.6(3)	86.2±3.4(3)	89.4±0.8*(3)
42	(100)	89.2±1.1(3)	88.9±2.0(3)	85.9±3.5(4)	90.2±0.6(3)
43	(50)	84.7±0.9**(3)	80.2±3.0**(3)	74.6±1.7***(3)	80.5±4.2**(3)
44	(100)	88.7±1.5(3)	87.4±1.6(3)	83.8±2.8(4)	89.2±0.5**(3)
	Control	92.3±0.3(3)	91.0±1.5(3)	89.5±0.6(4)	94.7±1.8(3)
45	(100)	89.8±0.3***(3)	85.7±3.5(3)	87.4±0.8(3)	92.9±2.3(3)
	Control	88.5±1.2(4)	87.2±0.5(5)	90.3±0.5(3)	89.4±0.3(4)
46	(100)	87.8±1.7(3)	85.1±1.7	87.0±1.0*(3)	88.7±0.9(3)
47	(100)	87.8±2.2(3)	82.0±0.4***(3)	87.3±0.5**(3)	88.3±1.8(3)
48	(100)	89.6±1.5(3)	83.2±1.6*(3)	88.5±1.8	87.9±0.5*(3)
50	(100)	88.3±1.2(3)	82.0±0.4***(3)	87.7±0.4**(3)	86.5±1.1*(3)
51	(100)	86.7±1.8(3)	82.4±1.8**(3)	87.9±0.6*(3)	87.2±0.8*(3)
52	(100)	85.4±2.6(3)	78.9±2.9**(3)	85.1±1.5**(3)	87.2±1.2***(3)
	Control	92.7±0.6(3)	88.2±0.3(4)	90.6±0.4(4)	91.1±0.9(4)
53	(100)	91.7±0.8(3)	82.8±0.5***(3)	84.4±1.1***(3)	82.7±6.0(4)
Aspirin	IC_{50}		20.0 μM		

Platelet were incubated with tested sample or 0.5% DMSO at 37 ℃ for 1min, then thrombin (0.1 U/ml), AA (100 μM), collagen (10 μg/ml) or PAF (2 ng/ml) was added to trigger the aggregation. Values are presented as mean±S.E. , N=3-5. *: P<0.05, **: P<0.01, ***: P<0.001.

Table 3. The inhibitory effect of substituted furo[2,3-*b*]chromone-2-carboxylic acid ethyl esters on rabbit platelet aggregation induced by thrombin, AA, collagen and PAF (*in vitro*)



61: $R_1=R_2=R_3=R_4=H$ **67**: $R_1=R_2=R_4=H$, $R_3=OCH_3$

62: $R_1=R_2=R_3=H$, $R_4=CH_3$ **68**: $R_1=R_3=R_4=H$, $R_2=OCH_3$

63: $R_1=R_2=R_4=H$, $R_3=CH_3$ **70**: $R_1=R_2=R_4=H$, $R_3=Cl$

64: $R_1=R_3=R_4=H$, $R_2=CH_3$ **71**: $R_1=R_3=R_4=H$, $R_2=Cl$

65: $R_2=R_3=R_4=H$, $R_1=CH_3$ **72**: $R_1=R_3=R_4=H$, $R_2=Br$

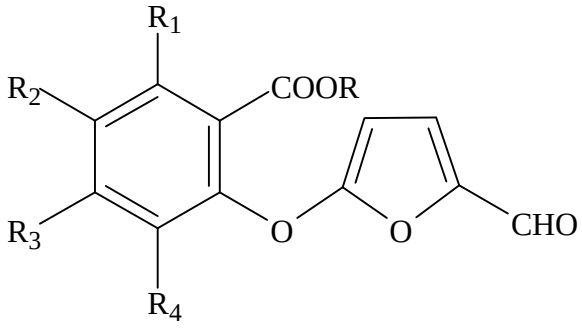
66: $R_1=R_2=R_3=H$, $R_4=OCH_3$ **73**: $R_1=R_3=R_4=H$, $R_2=I$

Compound	conc. (μg/ml)	Percent Aggregation: thrombin	AA	collagen	PAF
	Control	93.4±1.5(4)	88.9±0.5(4)	91.2±0.6(4)	91.4±0.2(4)
61	(100)	83.3±2.7**(3)	0.0±0.0***(4)	46.3±4.8***(4)	66.0±9.8*(4)
	(50)		0.0±0.0***(4)	53.5±12.3**(4)	
	(20)		4.6±4.0***(4)	79.8±7.0(4)	
	(10)		38.1±19.1*(4)		
	(5)		83.1±2.5*(4)		
	IC_{50}		55.1 μM	296.2 μM	
62	(50)	85.1±3.4*(3)	24.3±10.2***(4)	48.3±5.7***(4)	79.6±2.2***(3)
	(20)		18.5±16.0***(4)	67.3±14.2(4)	
	(10)		32.1±17.9**(4)	80.9±8.5(4)	
	(5)		60.7±9.6*(4)		
	(2)		83.8±2.0*(4)		
	IC_{50}		55.5 μM	165.9 μM	
63	(50)	cause spontaneous aggregation	46.8±6.1		
	(20)	90.4±1.9(3)	48.2±16.9*(4)	81.4±2.1***(3)	83.8±0.6***(3)
	(10)		72.7±6.2*(4)		
	(5)		85.4±1.5*(4)		

	IC_{50}		119.6 μM		
64	(100)	86.8±2.5*(3)	0.0±0.0***(3)	70.9±4.3***(4)	81.7±1.5***(3)
	(50)		0.0±0.0***(3)		
	(20)		1.4±1.2***(3)		
	(10)		19.0±15.5***(3)		
	(5)		32.3±21.8**(3)		
	(2)		84.4±1.9*(3)		
	IC_{50}		37.6 μM		
	Control	92.5±0.7(3)	91.3±0.7(3)	89.4±0.6(3)	91.5±0.7(3)
65	(100)	91.7±0.8(3)	83.5±1.1***(3)	74.9±1.9***(3)	87.7±0.2***(3)
66	(50)	89.2±0.8*(3)	77.0±1.4***(3)	75.0±3.1***(3)	87.5±0.5***(3)
67	(50)	89.6±1.0*(3)	57.0±5.1***(3)	66.4±4.6***(3)	86.1±0.7***(3)
68	(50)	88.3±0.8**(3)	49.7±3.0***(3)	8.2±1.8***(3)	72.9±0.7***(3)
	(20)			15.6±4.8***(3)	
	(10)			55.5±9.4**(3)	
	(5)			81.8±1.1***(3)	
	IC_{50}			58.9 μM	
	Control	88.2±0.5(4)	87.7±0.2(4)	87.7±0.4(4)	89.8±0.6(4)
70	(30)	85.2±0.3***(3)	82.4±1.4***(3)	84.9±0.6**(4)	89.5±1.0(3)
71	(30)	86.0±2.1(3)	85.3±1.5(3)	62.2±16.7(4)	87.4±1.2(3)
72	(100)	86.2±1.3(3)	0.0±0.0***(3)	2.0±1.8***(4)	84.3±2.1*(3)
	(50)		0.0±0.1***(3)	9.1±1.5***(4)	
	(20)		26.4±3.0***(3)	27.8±6.4***(4)	
	(10)		69.5±2.5***(3)	84.6±1.0*(4)	
	(5)		83.7±1.3***(3)		
	IC_{50}		55.4 μM	88.0 μM	
73	(100)	85.5±1.6(3)	11.7±2.7***(3)	5.6±1.0***(3)	86.7±1.6(3)
	(20)		44.3±5.1***(3)	81.0±0.1***(3)	
	(10)		80.5±0.2***(3)		
	IC_{50}		103.4 μM		
Aspirin	IC_{50}		20.0 μM		

Platelet were incubated with tested sample or 0.5% DMSO at 37 ℃ for 1min, then thrombin (0.1 U/ml), AA (100 μM), collagen (10 μg/ml) or PAF (2 ng/ml) was added to trigger the aggregation. Values are presented as mean±S.E. , N=3-4. *: P<0.05, **: P<0.01, ***: P<0.001.

Table 4. The inhibitory effect of 5-(2'-alkoxycarbonyl substituted phenoxy)furfurals on human platelet aggregation induced by thrombin, AA and collagen (*in vitro*)



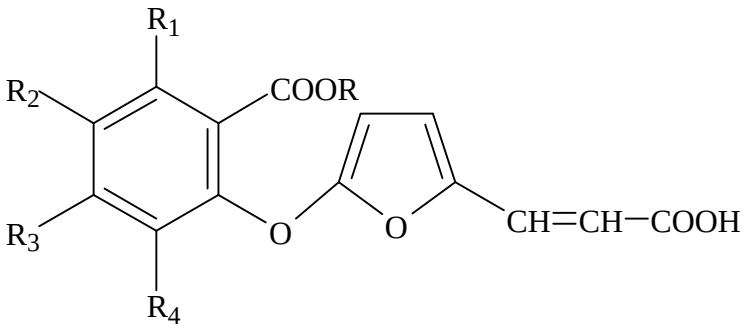
81: R=CH_3, R_1=R_2=R_3=R_4=H
82: R=CH_3, R_1=R_2=R_3=H, R_4=CH_3
83: R=CH_3, R_1=R_2=R_4=H, R_3=CH_3
84: R=CH_3, R_1=R_3=R_4=H, R_2=CH_3
85: R=C_2H_5, R_2=R_3=R_4=H, R_1=CH_3
86: R=CH_3, R_1=R_2=R_3=H, R_4=OCH_3
87: R=CH_3, R_1=R_2=R_4=H, R_3=OCH_3
88: R=CH_3, R_1=R_3=R_4=H, R_2=OCH_3
89: R=CH_3, R_2=R_3=R_4=H, R_1=OCH_3
90: R=CH_3, R_1=R_2=R_4=H, R_3=Cl
91: R=CH_3, R_1=R_3=R_4=H, R_2=Cl
92: R=CH_3, R_1=R_3=R_4=H, R_2=Br
93: R=CH_3, R_1=R_3=R_4=H, R_2=I

Compound	conc. (μg/ml)	Percent Aggregation: thrombin	AA	collagen
	Control	85.5±1.19 (10)	85.96±1.72 (7)	91.3±1.3 (6)
81	(150)	81.1±2.74 (5)	11.75±4.85 (4)	87.7±0.87 (3)
82	(150)	40.16±5.9 (5)	80.3±6.29 (3)	88.0±1.70 (3)
83	(150)	29.7±3.9 (6)	14.84±2.85 (5)	90.0±1.17 (3)
84	(150)	24.53±4.85 (4)	38.2±1.58 (3)	86.5±1.14 (3)
85	(200)	36.78±6.73 (4)	1.43±1.17 (3)	88.7±2.94 (3)
	(100)		88.5±0.46 (2)	
	Control	90.37±1.2 (7)	86.6±2.19 (6)	84.5±2.0 (6)
86	(200)	90.47±0.31 (3)	5.10±4.16 (3)	52.58±5.59 (4)
	(100)		88.73±1.37 (3)	84.5±3.19 (3)
87	(200)	90.4±1.77 (3)	5.53±2.26 (3)	35.73±1.89 (4)
	(100)		87.67±0.38 (3)	63.57±9.05 (3)
	(50)			83.63±3.30 (3)
	IC_{50}			156.3 μM
88	(200)	90.6±1.69 (3)	0.0±0.0 (3)	35.35±0.85 (4)
	(100)		84.33±2.0 (3)	75.57±6.01 (3)

	Control	85.5±1.19 (10)	85.96±1.72 (7)	91.3±1.3 (6)
89	(200)	29.17±1.1 (3)	63.2±10.53 (4)	88.7±1.55 (3)
	Control	90.37±1.2 (7)	86.6±2.19 (6)	84.5±2.0 (6)
90	(200)	89.53±1.65 (3)	11.7±2.78 (3)	34.28±0.91 (4)
	(100)		53.6±0.5 (3)	74.83±4.16 (3)
	(50)		85.2±0.99 (3)	
	IC_{50}		112.5 μM	
91	(200)	81.17±5.28 (3)	11.83±1.65 (3)	35.06±4.56 (3)
	(100)		89.53±0.58 (4)	19.0±15.51 (3)
	(50)			85.33±1.69 (3)
	IC_{50}			105.5 μM
92	(200)	87.63±1.09 (3)	5.4±2.84 (3)	28.95±2.61 (4)
	(100)		0.0±0.0 (3)	37.87±1.69 (3)
	(50)		87.0±0.9 (3)	83.87±4.36 (3)
	IC_{50}		74.9 μM	115.3 μM
93	(200)	84.7±2.6 (3)	19.93±4.13 (4)	36.13±4.37 (4)
	(100)		0.0±0.0 (3)	46.87±0.78 (3)
	(50)		84.1±0.77 (3)	83.23±1.1 (3)
	IC_{50}		69.4 μM	104.4 μM

Platelet were incubated with tested sample or 0.5% DMSO at 37 ℃ for 1min, then thrombin (0.1 U/ml), AA (200 μM) and collagen (10 μg/ml) was added to trigger the aggregation. Values are presented as mean±S.E. , N=2-10.

Table 5. The inhibitory effect of 5-(2'-alkoxycarbonyl substituted phenoxy)-2-furanacrylic acids on human platelet aggregation induced by thrombin, AA and collagen (*in vitro*)

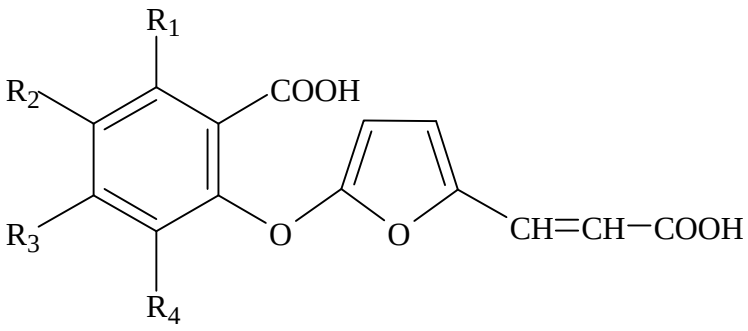


101: R=CH_3, R_1=R_2=R_3=R_4=H
102: R=CH_3, R_1=R_2=R_3=H, R_4=CH_3
103: R=CH_3, R_1=R_2=R_4=H, R_3=CH_3
104: R=CH_3, R_1=R_3=R_4=H, R_2=CH_3
105: R=C_2H_5, R_2=R_3=R_4=H, R_1=CH_3
106: R=CH_3, R_1=R_2=R_3=H, R_4=OCH_3
107: R=CH_3, R_1=R_2=R_4=H, R_3=OCH_3
108: R=CH_3, R_1=R_3=R_4=H, R_2=OCH_3
109: R=CH_3, R_2=R_3=R_4=H, R_1=OCH_3

Compound	conc. (μg/ml)	Percent Aggregation		
		thrombin	AA	collagen
	Control	85.5±1.19 (10)	85.96±1.72 (7)	91.3±1.3 (6)
101	(200)	72.0±7.3 (4)	62.27±15.95 (3)	89.2±1.06 (3)
102	(200)	52.08±10.9 (5)	49.7±14.9 (3)	89.2±1.09 (3)
103	(200)	88.1±1.2 (3)	73.8±10.0 (3)	35.1±5.0 (3)
	(100)			64.3±10.4 (3)
104	(200)	78.7±5.1 (4)	15.2±2.33 (3)	86.8±1.11 (3)
	(100)		89.5±0.21 (2)	
105	(200)	84.7±0.1 (3)	89.2±1.09 (3)	90.2±0.63 (3)
	Control	90.37±1.2 (7)	86.6±2.19 (6)	84.5±2.0 (6)
106	(200)	92.33±2.1 (3)	64.83±10.49 (3)	78.95±3.87 (4)
107	(200)	92.87±1.11 (3)	81.17±4.36 (3)	78.8±3.68 (4)
108	(200)	91.83±1.61 (3)	73.7±4.72 (3)	84.9±1.64 (4)
109	(200)	90.53±3.4 (3)	62.43±12.15 (3)	76.15±8.66 (4)

Platelet were incubated with tested sample or 0.5% DMSO at 37 ℃ for 1min, then thrombin (0.1 U/ml), AA (200 μM) and collagen (10 μg/ml) was added to trigger the aggregation. Values are presented as mean±S.E. , N=2-10.

Table 6. The inhibitory effect of 5-(2'-carboxyl substituted phenoxy)-2-furanacrylic acids on human platelet aggregation induced by thrombin, AA and collagen (*in vitro*)



111: $R_1=R_2=R_3=R_4=H$
112: $R_1=R_2=R_3=H$, $R_4=CH_3$
113: $R_1=R_2=R_4=H$, $R_3=CH_3$
114: $R_1=R_3=R_4=H$, $R_2=CH_3$
116: $R_1=R_2=R_3=H$, $R_4=OCH_3$
117: $R_1=R_2=R_4=H$, $R_3=OCH_3$
118: $R_1=R_3=R_4=H$, $R_2=OCH_3$
120: $R_1=R_2=R_4=H$, $R_3=Cl$
121: $R_1=R_3=R_4=H$, $R_2=Cl$
122: $R_1=R_3=R_4=H$, $R_2=Br$
123: $R_1=R_3=R_4=H$, $R_2=I$

Compound	conc. (μg/ml)	Percent Aggregation: thrombin	AA	collagen
	Control	85.5±1.19 (10)	85.96±1.72 (7)	91.3±1.3 (6)
111	(200)	82.92±3.6 (5)	84.92±1.66 (5)	89.0±1.21 (3)
112	(200)	91.6±0.29 (3)	88.5±0.8 (3)	87.0±0.96 (3)
113	(200)	73.0±3.52 (4)	46.67±16.77 (3)	87.9±1.12 (3)
114	(200)	89.8±0.9 (3)	89.6±0.45 (3)	88.9±1.58 (3)
	Control	90.37±1.2 (7)	86.6±2.19 (6)	84.5±2.0 (6)
116	(200)	91.97±1.98 (3)	56.93±15.79 (3)	86.68±1.37 (4)
117	(200)	94.05±0.81 (2)	72.73±2.62 (3)	78.17±7.75 (3)
118	(200)	94.60±0.0 (2)	82.77±2.78 (3)	87.4±1.5 (3)
120	(200)	90.4±1.58 (3)	12.85±6.05 (3)	61.52±7.98 (4)
	(100)		84.63±1.59 (3)	
121	(200)	89.7±2.29 (3)	63.35±12.83 (2)	69.06±8.03 (5)
122	(200)	91.63±1.76 (3)	31.3±16.26 (4)	62.25±3.46 (4)
	(100)		86.53±1.14 (3)	
123	(200)	91.07±1.32 (3)	0.0±0.0 (3)	37.73±1.92 (4)
	(100)	40.0±6.94 (3)	40.0±6.94 (3)	43.47±0.83 (3)
	(50)	81.67±1.96 (3)	81.67±1.96 (3)	85.53±1.65 (3)

IC_{50}	97.9 μM	134.5 μM

Platelet were incubated with tested sample or 0.5% DMSO at 37 ℃ for 1min, then thrombin (0.1 U/ml), AA (200 μM) and collagen (10 μg/ml) was added to trigger the aggregation. Values are presented as mean±S.E. , N=2-10.