Electronic Supplementary Material (ESI) for RSC Advances.

Characterization data of synthesized compounds:

3-(4'-methoxy)phenyl-1-(4-biphenyl)propen-1-one (1a): M.pt. 122-124^{0}C; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 8.1 (d, 1H, CH=CH, 15.3 Hz), 7.4 (d, 1H, CH=CH, 15.3 Hz), 7.2-8.5 (m, 13 H, Ar-H), 3.9 (s, 3H, OCH_3), IR (KBr, cm^{-1}) 3189 (C-H aromatic stretch), 1652 (C=O stretch), 1597 (C=C Stretch).

3-(4'-nitro)phenyl-1-(4-biphenyl)propen-1-one (1b): M.pt. 189-191^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ, ppm) 7.54 (d, 1H, CH=CH, 15.3 Hz), 7.2 (d, 1H, CH=CH, 15.3 Hz), 7.1-8.45 (m, 13 H, Ar-H), IR (KBr, cm^{-1}) 3089 (C-H aromatic stretch), 1650 (C=O stretch), 1597 (C=C Stretch), 1550 &1350 (NO_2 stretch).

3-(4'-chloro)phenyl-1-(4-biphenyl)propen-1-one (1c): M.pt. 183-185^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ, ppm) 8.06 (d, 1H, CH=CH, 15.7 Hz), 7.34 (d, 1H, CH=CH, 15.7 Hz), 7.18-8.46 (m, 13 H, Ar-H), IR (KBr, cm^{-1}) 3020 (C-H aromatic stretch), 1652 (C=O stretch), 1598 (C=C Stretch).

3-(4'-fluoro)phenyl-1-(4-biphenyl)propen-1-one (1d): M.pt. 193-195^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ) 7.52 (d, 1H, CH=CH, 15.3 Hz), 7.1-8.45 (m, 13H, Ar-H), 6.95 (d, 1H, CH=CH, 15.3 Hz), IR (KBr, cm^{-1}) 3020 (C-H aromatic stretch), 1650 (C=O stretch), 1585 (C=C Stretch).

3-(4'-dimethylamino)phenyl-1-(4-biphenyl)propen-1-one (1e): M.pt. 160-162^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ) 7.88 (d, 1H, CH=CH, 15.1 Hz), 7.4 (d, 1H, CH=CH, 15.1Hz), 7.18-8.41 (13H,m,Ar-H), IR (KBr, cm^{-1}) 3080 (C-H aromatic stretch), 1649 (C=O stretch), 1591 (C=C Stretch).

3-(3'-methoxy)phenyl-1-(4-biphenyl)propen-1-one (1f): M.pt. 138-140^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ) 7.84 (d, 1H, CH=CH, 15.8 Hz), 7.44 (d, 1H, CH=CH, 15.8 Hz), 7.16-8.46 (m, 13H, Ar-H), 3.82 (s, 3H, OCH_3), IR (KBr, cm^{-1}) 3125 (C-H aromatic stretch), 1656 (C=O stretch), 1599 (C=C Stretch).

3-(3'-nitro) phenyl-1-(4-biphenyl)propen-1-one (1g): M.pt.183-184^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ) 7.7 (d, 1H, CH=CH, 15.3 Hz), 7.4 (d, 1H, CH=CH, 15.3 Hz), 7.1-8.34 (m, 13H, Ar-H), IR (KBr, cm^{-1}) 3095 (C-H aromatic stretch), 1651 (C=O stretch), 1595 (C=C Stretch).

3-(2'-methoxy)phenyl-1-(4-biphenyl)propen-1-one (1h): M.pt. 158-160^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ) 3.86 (s, 3H, OCH_3), 7.88 (d, 1H, CH=CH, 15.7 Hz), 7.45 (d, 1H,

CH=CH, 15.7 Hz), 7.12-8.5 (m, 13H, Ar-H), IR (KBr, cm^{-1}) 3035 (C-H aromatic stretch), 1652 (C=O stretch), 1598 (C=C Stretch).

3-phenyl-1-(4-biphenyl)propen-1-one (1i): M.pt. 140-142^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ) 7.9 (d, 1H, CH=CH, 15.7 Hz), 7.62 (d, 1H, CH=CH, 15.7 Hz), 7.22-7.87 (m, 13H, Ar-H), IR (KBr, cm^{-1}) 3045 (C-H aromatic stretch), 1655 (C=O stretch), 1590 (C=C Stretch).

1-Formyl-3-(4-biphenyl)-5-(4'-methoxyphenyl)-2-pyrazoline (2a). M. Pt. 166-168^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ ppm), 4.09 (1H, dd, CH_2, pyrazoline), 4.29 (1H, dd, CH_2, pyrazoline), 5.53 (1H, dd, , CH, pyrazoline), 6.89-8.27 (m, 13 H, Ar-H), 8.89 (1H, s, CHO), IR (KBr, cm^{-1}), 1597 (C=N Stretch), 1659 (C=O stretch), 2885 & 2745 (C-H aldehyde stretch)

1-Formyl-3-(4-biphenyl)-5-(4'-nitrophenyl)-2-pyrazoline (2b). M.Pt. 154-156^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.2 (1H, dd, CH_2, pyrazoline), 3.9 (1H, dd, CH_2, pyrazoline), 5.55 (1H, dd, , CH, pyrazoline), 7.4-8.2 (m, 13 H, Ar-H), 8.94 (1H, s, CHO), IR (KBr, cm^{-1}) 1597 (C=N Stretch), 1659 (C=O stretch), 2793 & 2708 (C-H aldehyde stretch)

1-Formyl-3-(4-biphenyl -5- (4'-chlorophenyl)-2-pyrazoline (2c). M.Pt. 176-178^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.1 (1H, dd, CH_2, pyrazoline), 3.9 (1H, dd, CH_2, pyrazoline), 5.58 (1H, dd, , CH, pyrazoline), 7.1-8.4 (m, 13 H, Ar-H), 8.9 (1H, s, CHO), IR (KBr, cm^{-1}) 1597 (C=N Stretch), 1674 (C=O strech), 2816 & 2735 (C-H aldehyde stretch)

1-Formyl-3-(4-biphenyl-5-(4'-fluorophenyl)-2-pyrazoline (2d). M.Pt. 158-160^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.17 (1H, dd, CH_2, pyrazoline), 3.85 (1H, dd, CH_2, pyrazoline), 5.5 (1H, dd, CH, pyrazoline), 7.09-8.15 (m, 13 H, Ar-H), 8.85 (1H, s, CHO), IR (KBr, cm^{-1})

1-Formyl-3-(4-biphenyl -5-(4'-dimethylaminophenyl)-2-pyrazoline (2e). M.Pt. 179-180^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.3 (1H, dd, CH_2, pyrazoline), (6H, s, $N(CH_3)_2$), 3.9 (1H, dd, CH_2, pyrazoline), 5.4 (1H, dd, , CH, pyrazoline), 6.58-8.5 (m, 13 H, Ar-H), 8.9 (1H, s, CHO), IR (KBr, cm^{-1}) 1605 (C=N Stretch), 1674 (C=O stretch), 2908 & 2816 (C-H aldehyde stretch)

1-Formyl-3-(4-biphenyl -5-(3'-methoxyphenyl)-2-pyrazoline (2f). M.Pt. 138-140^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.17 (1H, dd, CH_2, pyrazoline), 3.85 (1H, dd, CH_2, pyrazoline), 5.5 (1H, dd, , CH, pyrazoline), 7.4-8.15 (m, 13 H, Ar-H), 8.9 (1H, s, CHO), IR (KBr, cm^{-1}) 1589 (C=N Stretch), 1659 (C=O stretch), 2924 & 2820 (C-H aldehyde stretch)

1-Formyl-3-(4-biphenyl)-5-(3'-nitrophenyl)-2-pyrazoline (2g). M. Pt. 146-148^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 4.02 (1H, dd, CH_2, pyrazoline), 4.25 (1H, dd, CH_2, pyrazoline), 5.5 (1H, dd, , CH, pyrazoline), 6.89-8.25 (m, 13 H, Ar-H), 8.89 (1H, s, CHO), IR (KBr, cm^{-1}) 1595 (C=N Stretch), 1659 (C=O stretch), 2790 & 2702 (C-H aldehyde stretch)

1-Formyl-3-(4-biphenyl)-5-(2'-methoxyphenyl)-2-pyrazoline (2h). M.Pt. 120-124^{0}C ; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.1 (1H, dd, CH_2, pyrazoline), 3.2 (3H, s, OCH_3), 3.8 (1H, dd, CH_2, pyrazoline), 5.6 (1H, dd, , CH, pyrazoline), 7.1-8.5 (m, 13 H, Ar-H), 8.9 (1H, s, CHO), IR (KBr, cm^{-1}) 1589 (C=N Stretch), 1659 (C=O stretch), 2820 & 2705 (C-H aldehyde stretch)

1-Formyl-3-(4-biphenyl)-2-pyrazoline, 2i. M.Pt. 125-126^{0}C ; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.25 (1H, dd, CH_2, pyrazoline), 3.78 (1H, dd, CH_2, pyrazoline), 5.45 (1H, dd, , CH, pyrazoline), 7.1-8.2(m, 13 H, Ar-H), 8.85 (1H, s, CHO), IR (KBr, cm^{-1}) 1585 (C=N Stretch), 1659 (C=O stretch), 2820 & 2710 (C-H aldehyde stretch)

1-Phenyl-3-(4-biphenyl)-5-(4'-methoxyphenyl)-2-pyrazoline (3a). M.Pt. 118-120^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.3 (1H, dd, CH_2, pyrazoline), 3.71 (s, 3H, OCH_3), 3.9 (1H, dd, CH_2, pyrazoline 5.4 (1H, dd, , CH, pyrazoline), 6.58-8.5 (m, 18 H, Ar-H) IR (KBr, cm^{-1}) 1602 (C=N stretch)

1-Phenyl-3-(4-biphenyl)-5-(4'-nitrophenyl)-2-pyrazoline (3b). M.Pt. ^{0}C ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.3 (1H, dd, CH_2, pyrazoline), 3.9 (1H, dd, CH_2, pyrazoline), 5.4 (1H, dd, CH, pyrazoline), 6.58-8.5 (m, 18 H, Ar-H) IR (KBr, cm^{-1}) 1597 (C=N stretch)

1-Phenyl-3-(4-biphenyl)-5-(4'-chlorophenyl)-2-pyrazoline (3c). M.Pt. 132-136^0; ^{1}H NMR (300MHz, $CDCl_3$, δ 3.3 (1H, dd, CH_2, pyrazoline),3.9 (1H, dd, CH_2, pyrazoline),), 5.4 (1H, dd, , CH, pyrazoline), 6.58-8.5 (m, 18 H, Ar-H) IR (KBr, cm^{-1}) 1585 (C=N stretch)

1-Phenyl-3-(4-biphenyl)-5-(4'-fluorophenyl)-2-pyrazoline (3d). M.Pt.166-169^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.19 (1H, dd, CH_2, pyrazoline), 3.99 (1H, dd, CH_2, pyrazoline), 5.5 (1H, dd, CH, pyrazoline), 7.28-8.14 (m, 18 H, Ar-H) IR (KBr, cm^{-1}) 1589 (C=N Strech)

1-Phenyl-3-(4-biphenyl -5-(4'-dimethylaminophenyl)-2-pyrazoline (3e). M.Pt.179-181 ^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.022 (6H, s, $N(CH_3)_2$), 3.14 (1H, dd, CH_2, pyrazoline), 3.89 (1H, dd, CH_2, pyrazoline), 5.41 (1H, dd, CH, pyrazoline), 6.66-7.84 (m, 18 H, Ar-H) IR(KBr,cm^{-1}) 1605 (C=N stretch)

1-Phenyl-3-(4-biphenyl -5-(3'-methoxyphenyl)-2-pyrazoline (3f). M.Pt. 134-136^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.25 (1H, dd, CH_2, pyrazoline), 3.65 (s, 3H, OCH_3), 3.65 (1H, dd, CH_2, pyrazolines), 5.25 (1H, dd, CH, pyrazoline), 6.50-8.25 (m, 18 H, Ar-H) IR (KBr, cm^{-1}) 1602 (C=N stretch)

1-Phenyl-3-(4-biphenyl-5-(3'-nitrophenyl)-2-pyrazoline (3g). M.Pt. 173-175^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.18(1H, dd, CH_2, pyrazoline), 3.96 (1H, dd, CH_2, pyrazoline), 5.4 (1H, dd, , CH, pyrazoline), 7.19-8.25 (m, 18H, Ar-H), IR (KBr, cm^{-1}) 1589 (C=N stretch)

1-Phenyl-3-(4-biphenyl -5-(2'-methoxyphenyl)-2-pyrazoline (3h). M.Pt. 155-156^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.15 (1H, dd, CH_2, pyrazoline), 3.6 (s, 3H, OCH_3), 3.55 (1H, dd, CH_2, pyrazolines, 5.05 (1H, dd, , CH, pyrazoline), 6.55-8.35 (m, 18 H, Ar-H), IR (KBr, cm^{-1}) 1597 (C=N strech)

1-Phenyl-3-(4-biphenyl) -5-pyrazoline (3i). M.Pt. 205-206^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.35 (1H, dd, CH_2, pyrazoline), 3.95 (1H, dd, CH_2, pyrazolines, 5.55 (1H, dd, CH, pyrazoline), 6.71-7.2 (m, 18 H, Ar-H), IR (KBr, cm^{-1}) 1597 (C=N strech)

3-(4-biphenyl -5-(4'-methoxyphenyl)-2-pyrazoline (4a). M.Pt. 158^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.19 (1H, dd, CH_2, pyrazoline), 3.89-3.99 (4H, m, 3H for OMe & CH_2, pyrazoline), 5.4 (1H, dd, , CH, pyrazoline), 7.14-8.01 (m, 13 H, Ar-H), 8.9 (1H, s, NH) IR (KBr, cm^{-1}) 1605 (C=N), 3340 (NH stretch)

3-(4-biphenyl -5-(4'-nitrophenyl)-2-pyrazoline (4b). M.Pt.178-180 ^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.0 (1H, dd, CH_2, pyrazoline), 3.55 (1H, dd, CH_2, pyrazoline), 4.85(1H, dd, , CH, pyrazoline), 7.17-7.95 (m, 13 H, Ar-H), 8.05 (1H, s, NH) IR (KBr, cm^{-1}) 1589 (C=N stretch), 3190 (NH stretch)

3-(4-biphenyl -5-(4'-chlorophenyl)-2-pyrazoline (4c). M.Pt.124^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.3 (1H, dd, CH_2, pyrazoline), (6H, s, $N(CH_3)_2$), 3.9 (1H, dd, CH_2, pyrazoline), 5.4 (1H, dd, , CH, pyrazoline), 6.58-8.5 (m, 13 H, Ar-H), 8.9 (1H, s, NH), IR (KBr, cm^{-1})1602 (C=N stretch), 3243 (NH stretch)

3-(4-biphenyl)-5-(4'-fluorophenyl)-2-pyrazoline (4d). M.Pt.136-138^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.03 (1H, dd, CH_2, pyrazoline), 3.51 (1H, dd, CH_2, pyrazoline), 4.94 (1H, dd, , CH, pyrazoline), 7.2-7.9 (m, 13 H, Ar-H), 8.09 (1H, s, NH), IR (KBr, cm^{-1}) 1597 (C=N stretch), 3189 (NH stretch)

3-(4-biphenyl)-5-(4'-dimethylaminophenyl)-2-pyrazoline (4e). M.Pt.160-162^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.01 (1H, dd, CH_2, pyrazoline), 3.50 (1H, dd, CH_2, pyrazoline), 4.93 (1H, dd, , CH, pyrazoline), 7.2-7.9 (m, 13 H, Ar-H), 8.13 (1H, s, NH), IR (KBr, cm^{-1}) 1590 (C=N stretch), 3231 (NH stretch)

3-(4-biphenyl)-5-(3'-methoxyphenyl)-2-pyrazoline (4f). M.Pt.146-148^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.15 (1H, dd, CH_2, pyrazoline), 3.89-3.99 (4H, m, 3H for OMe & CH_2, pyrazoline), 5.36 (1H, dd, , CH, pyrazoline), 7.14-8.01 (m, 13 H, Ar-H), 8.85 (1H, s, NH), IR (KBr, cm^{-1}) 1602 (C=N strech), 3330 (NH stretch),

3-(4-biphenyl)-5-(3'-nitrophenyl)-2-pyrazoline (4g)**.** M.Pt. 170-172^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.0 (1H, dd, CH_2, pyrazoline), 3.62 (1H, dd, CH_2, pyrazoline), 5.21 (1H, dd, , CH, pyrazoline), 7.17-8.02 (m, 13 H, Ar-H), 8.2 (1H, s, NH), IR (KBr, cm^{-1}) 1585 (C=N stretch), 3190 (NH stretch)

3-(4-biphenyl)-5-(2'-methoxyphenyl)-2-pyrazoline (4h). M.Pt. 152-155^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.18 (1H, dd, CH_2, pyrazoline), 3.89-3.99 (4H, m, 3H for OMe & CH_2, pyrazoline), 5.37 (1H, dd, , CH, pyrazoline), 7.14-8.01 (m, 13 H, Ar-H), 8.85 (1H, s, NH), IR (KBr, cm^{-1}) 1592 (C=N strech), 3235 (NH stretch)

3-(4-biphenyl)-2-pyrazoline (4i). M.Pt. 125-128^{0}C; ^{1}H NMR (300MHz, $CDCl_3$, δ), 3.28 (1H, dd, CH_2, pyrazoline), 3.89 (1H, dd, CH_2, pyrazoline), 5.17 (1H, dd, , CH, pyrazoline), 7.14-7.98 (m, 13 H, Ar-H), 8.85 (1H, s, NH), IR (KBr, cm^{-1}) 1595 (C=N strech), 3230 (NH stretch)

Tables

Table-1: Effect of 4'-phenylchalcones (1), N-formylpyrazolines (2), N-phenylpyrazolines (3) and pyrazolines derivatives (4) on Endogenous Protein Hydrolysis.

S. No.	Compound	% Residual Activity	
		Endogenous protein Hydrolysis at 10^{-4} M	
		3 hr	24 hr
	Control	100±0.90	100±0.40
1.	(1a)	21.97±0.25	47.07±3.09
2.	(1b)	0±0.0	29.90±1.78

3.	**(1c)**	**30.19±0.92**	**50.30±3.45**
4.	**(1d)**	**0±0.0**	**26.06±1.15**
5.	**(1e)**	**0±0.0**	**40.00±0.22**
6.	**(1f)**	**12.01±1.23**	**55.90±0.56**
7.	**(1g)**	**67.99±1.82**	**86.06±2.99**
8.	**(1h)**	**30.12±1.56**	**70.10±2.0**
9.	**(1i)**	**25±0.0**	**67±0.0**
10.	**(2a)**	**33.05±0.23**	**82.42±5.33**
11.	**(2b)**	**23.01±0.71**	**77.98±3.53**
12.	**(2c)**	**32.33±1.97**	**97.98±1.27**
13.	**(2d)**	**70.08±1.59**	**95.96±3.62**
14.	**(2e)**	**71.97±5.79**	**98.99±0.30**
15.	**(2f)**	**50.00±3.09**	**98.18±0.76**
16.	**(2g)**	**48.32±1.07**	**91.92±2.93**
17.	**(2h)**	**0±0.0**	**10.39±0.24**
18.	**(2i)**	**35±1.57**	**88.18±0.76**
19.	**(3a)**	**0±0.0**	**20.00±0.31**
20.	**(3b)**	**42.05±1.99**	**86.06±1.98**
21.	**(3c)**	**5.00±0.38**	**31.92±0.85**
22.	**(3d)**	**0±0.0**	**46.06±2.36**
23.	**(3e)**	**38.07±1.67**	**80.00±3.55**
24.	**(3f)**	**0±0.0**	**42.02±0.87**
25.	**(3g)**	**0±0.0**	**65.05±0.78**
26.	**(3h)**	**12.99±1.15**	**88.89±6.61**
27.	**(3i)**	**36.05±1.99**	**40.05±1.09**
28.	**(4a)**	**56.90±3.68**	**71.92±3.27**
29.	**(4b)**	**87.03±0.71**	**92.93±1.29**
30.	**(4c)**	**73.01±0.48**	**94.95±0.70**

31.	**(4d)**	**51.05±2.36**	**92.93±3.80**
32.	**(4e)**	**57.95±1.11**	**93.94±0.83**
33.	**(4f)**	**48.95±0.29**	**86.06±0.54**
34.	**(4g)**	**0±0.00**	**46.90±3.08**
35.	**(4h)**	**36.07±1.07**	**57.90±2.68**
36.	**(4i)**	**58.11±1.55**	**65.90±2.8**

the results are present as % residual activitives in 0.1% liver homogenate of the experiment conducted in triplicate w.r.to control where no compound was added but equivalent amount of dmso was present. the valuesin parenthesis indicate the lower concentrations of inhibitor at which the enzyme activities were determined.

Table-2: Effect of 4'-phenylchalcones (1), N-formylpyrazolines (2), N-phenylpyrazolines (3) and pyrazolines derivatives (4) on Cathepsin B, Cathepsin H and Cathepsin L activities.

S. No.	Compound	% Residual Activity		
		Cathepsin B	Cathepsin H	Cathepsin L
	Control	**100±1.77**	**100±0.670**	**100±0.780**
1.	**(1a)**	**17±1.17**	**24.03±0.49**	**94±0.517**
2.	**(1b)**	**26±1.90**	**34.05±2.22**	**47±0.38**
3.	**(1c)**	**28±1.91**	**48.00±0.46**	**64±0.40**
4.	**(1d)**	**31±1.93**	**25.00±1.22**	**75±0.74**
5.	**(1e)**	**21±1.54**	**18.00±1.57**	**80±0.61**
6.	**(1f)**	**22±1.90**	**40.00±0.43**	**85±0.58**
7.	**(1g)**	**27±1.62**	**34.05±2.94**	**58±0.34**
8.	**(1h)**	**31.68±1.45**	**43.51±0.92**	**90±0.90**
9.	**(1i)**	**82±1.19**	**65±0.715**	**82±0.74**
10.	**(2a)**	**90±0.12**	**68.11±1.49**	**95±1.42**
11.	**(2b)**	**53.5±1.2(0.1)**	**28.91±2.92**	**35±0.38**
12.	**(2c)**	**70±0.0**	**22.13±2.05**	**80±0.80**
13.	**(2d)**	**60±0.28**	**48.11±1.38**	**70±0.63**

14.	**(2e)**	**94±0.0**	**35.67±2.65**	**84±1.22**
15.	**(2f)**	**93±0.40**	**53.78±3.81**	**90±1.11**
16.	**(2g)**	**56±1.97(0.1)**	**61.08±3.11**	**50±0.72**
17.	**(2h)**	**96±21.675**	**48.92±2.05**	**92±1.04**
18.	**(2i)**	**82±1.12**	**65±0.715**	**87±1.64**
19.	**(3a)**	**92±2.99**	**23.57±1.32**	**95±1.42**
20.	**(3b)**	**81.5±2.92**	**61.89±2.19**	**55±1.084**
21.	**(3c)**	**-**	**38.92±1.35(0.1)**	**77±0.94**
22.	**(3d)**	**87.5±3.55**	**12.89±2.32**	**75±1.17**
23.	**(3e)**	**-**	**54.86±3.30**	**72±0.82**
24.	**(3f)**	**95.5±3.36**	**9.94±0.78(0.1)**	**90±1.3**
25.	**(3g)**	**85.0±2.92**	**4.22±2.54(0.1)**	**70±1.24**
26.	**(3h)**	**98.6±3.74**	**34.86±2.05**	**82±1.45**
27.	**(3i)**	**60±0.72**	**72±0.972**	**79±1.49**
28.	**(4a)**	**40±3.46**	**88.11±3.86**	**84±0.96**
29.	**(4b)**	**34±1.47**	**85.40±5.70**	**50.5±0.63**
30.	**(4c)**	**67±2.35**	**90.00±4.13**	**74±1.07**
31.	**(4d)**	**60±2.13**	**50.00±2.05**	**70±1.24**
32.	**(4e)**	**79±2.07**	**81.89±1.92**	**80±1.34**
33.	**(4f)**	**73±3.73**	**68.11±2.65**	**82±1.10**
34.	**(4g)**	**49±2.0**	**70±0.56**	**65±1.09**
35.	**(4h)**	**80±3.72**	**56±0.98**	**83±1.47**
36.	**(4i)**	**81.0±0.132**	**67±1.005**	**90±1.33**
37.	**Leupeptin**	**1.14±0.62(0.001mM)**	**47.11±0.40(0.01mM)**	**11.5±0.35(10^{-9}M)**
38.	**Leu-CH_2-Cl**	**89.93±0.70(0.01mM)**	**6.31±0.45(0.01mM)**	**98.3±0.65(0.01mM)**

the % residual activities for cathepsin b in the series 1a-1i and 3a-3i were estimated at 10-5 m, 2a-2i and 4a-4i were at 10-6m.for cathepsin h estimated at 10-5m and for cathepsin l 1a-1i, 2a-2i were estimated at 10-9m and 3a-3i were at 10-6m, 4a-4iwere estimated at 10-8m.

Table 3 Inhibitory activities and K_i values of compounds with the substituted 4'-phenylchalcones against cathepsin B, cathepsin H and cathepsin L

		Cathepsin B		Cathepsin H		Cathepsin L	
Compound	**R**	**K_m, (10^{-3} M)**	**K_i (10^{-5} M)**	**V_{max},**	**K_i (10^{-5} M)**	**K_m,(10^{-3} M)**	**K_i(10^{-9}M)**
1a	p-OCH_3	4.08	0.124	1.6	0.44	0.062	12.98
1b	p-NO2	6.66	0.072	1.32	0.34	0.166	0.54
1c	p-Cl	3.63	0.141	1.57	0.42	0.086	2.08
1d	p-F	4.34	0.115	1.47	0.38	0.125	0.64
1e	p-$N(CH_3)_2$	5.12	0.096	1.66	0.46	0.1	1.38
1f	m-OCH_3	4.88	0.102	1.40	0.36	0.083	2.32
1g	m-NO_2	4.06	0.124	1.55	0..42	0.142	0.69
1h	o-OCH_3	4.85	0.102	1.50	0.4	0.071	4.46
1i	H	3.05	0.173	2.27	0.76	0.09	1.82
	R	**K_m, (10^{-3} M)**	**K_i (10^{-7} M)**	**V_{max},**	**K_i (10^{-4} M)**	**K_m,(10^{-3} M)**	**K_i(10^{-9} M)**
2a	p-OCH_3	0.51	7.46	3.84	2.71	0.065	8.33
2b	p-NO2	2.38	0.236	4.76	9.52	0.28	0.26
2c	p-Cl	0.87	1.087	3.38	1.79	0.08	2.7
2d	p-F	0.83	1.19	2.15	0.69	0.09	1.82
2e	p-$N(CH_3)_2$	1.64	3.8	4.0	3.17	0.11	1.12
2f	m-OCH_3	1.61	3.9	4.34	4.73	0.074	3.70
2g	m-NO_2	1.49	0.43	2.27	0.76	0.181	0.89
2h	o-OCH_3	1.28	0.549	3.12	1.45	0.068	5.88
2i	H	0.62	1.02	3.03	1.36	0.078	2.90
Compound	**R**	**Km' (10^{-3} M)**	**K_i (10^{-4} M)**	**Km'(10^{-3} M)**	**K_i (10^{-4} M)**	**Km' (10^{-3} M)**	**K_i(10^{-8}M)**
3a	p-OCH_3	0.58	3.39	0.55	4.5	0.065	8.33
3b	p-NO2	4.00	0.126	0.60	3.03	0.15	0.63
3c	p-Cl	-	-	1.05	0.75	0.105	1.23

3d	p-F	1.42	0.46	1.145	0.64	0.097	1.49
3e	p-$N(CH_3)_2$	-	-	0.85	1.14	0.1	1.38
3f	m-OCH_3	0.55	4.50	0.60	1.51	0.064	10.7
3g	m-NO_2	3.84	0.132	0.50	9.09	0.117	0.98
3h	o-OCH_3	0.54	5.0	0.70	1.82	0.083	2.32
3i	H	0.91	0.978	0.95	0.90	0.086	2.08
Compound	**R**	**Km' (10^{-3} M)**	**Ki (10^{-6}M)**	**V_{max}'**	**K_i (10^{-5} M)**	**Km'(10^{-3} M)**	**Ki(10^{-8}M)**
4a	p-OCH_3	5.0	0.099	4.65	7.69	0.08	2.86
4b	p-NO2	6.66	0.072	4.57	6.75	0.18	0.48
4c	p-Cl	1.66	0.370	4.77	9.80	0.085	2.27
4d	p-F	2.22	0.254	2.38	0.826	0.09	1.9
4e	p-$N(CH_3)_2$	1.17	0.619	4.44	5.55	0.1	1.44
4f	m-OCH_3	1.25	0.562	4.16	3.846	0.081	2.84
4g	m-NO_2	4.0	0.126	3.77	2.538	0.125	0.90
4h	o-OCH_3	1.0	0.818	3.57	2.11	0.083	2.46
4i	H	3.25	0.16	3.17	1.52	0.064	10.7

the experiments for cathepsin b were conducted in triplicate using different concentrations of bana as substrate at ph 6.0 in presence of 1.0 x 10-5 m concentrations of various 4'-phenylchalcones, 1a-1i; n-formylpyrazolines, 2a-2i; n-phenylpyrazolines 3a-3i and pyrazolines 4a-4i. the results are calculated using line weaver-burk equation for competitive inhibitors. cathepsin h activity was measured using leuna as substrate at ph 7.0 at 1 x 10-5 m of 1a-1i, 2a-2i, 3a-3i, 4a-4i. the km value of bana for cathepsin b, leuβna for cathepsin h and phearg for cathepsin l was found to be 4.54 x 10-4 m, 4.0 x 10-4 m, 5.8 x10-5 m.

Table-4: Docking studies showing decrease in different energies of cathepsin B in presence of different 4'-phenylchalcones and their pyrazolines derivatives

#Ligand	Total Energy (kcal/mol)	VDW	HBond	Elec
cav2IPP B_PYS-ic1a-2.pdb	-81.48	-78.40	-3.07	0
cav2IPP B_PYS-ic1b-0.pdb	-83.30	-75.11	-8.18	0
cav2IPP B_PYS-ic1c-0.pdb	-80.44	-80.44	0	0
cav2IPP B_PYS-ic1d-1.pdb	-85.45	-77.42	-8.02	0
cav2IPP B_PYS-ic1e-2.pdb	-86.58	-78.19	-8.38	0
cav2IPP B_PYS-ic1f-2.pdb	-84.28	-84.28	0	0
cav2IPP B_PYS-ic1g-2.pdb	-88.96	-75.17	-13.78	0
cav2IPP B_PYS-ic1h-1.pdb	-90.44	-84.44	-6	0

cav2IPP B_PYS-ic1i-1.pdb	-77.80	-69.09	-8.71	0
cav2IPP B_PYS-i2a-2.pdb	-91.82	-74.10	-17.72	0
cav2IPP B_PYS-i2b-0.pdb	-89.11	-70.76	-18.34	0
cav2IPP B_PYS-i2c-1.pdb	-89.08	-74.73	-14.35	0
cav2IPP B_PYS-i2d-0.pdb	-86.39	-78.07	-8.32	0
cav2IPP B_PYS-i2e-0.pdb	-88.92	-74.42	-14.5	0
cav2IPP B_PYS-i2f-2.pdb	-93.96	-76.08	-17.88	0
cav2IPP B_PYS-i2g-2.pdb	-94.57	-78.76	-15.80	0
cav2IPP B_PYS-i2h-0.pdb	-95.34	-79.34	-16.00	0
cav2IPP B_PYS-i2i-1.pdb	-88.53	-80.10	-8.43	0
cav2IPP B_PYS-i3a-0.pdb	-100.35	-100.35	0	0
cav2IPP B_PYS-i3b-1.pdb	-99.42	-89.70	-8.31	-1.40
cav2IPP B_PYS-i3c-0.pdb	-97.78	-89.28	-8.5	0
cav2IPP B_PYS-i3d-2.pdb	-96.78	-88.28	-8.5	0
cav2IPP B_PYS-i3e-2.pdb	-98.41	-89.94	-8.46	0
cav2IPP B_PYS-i3f-0.pdb	-98.28	-89.78	-8.5	0
cav2IPP B_PYS-i3g-2.pdb	-100.21	-82.29	-17.92	0
cav2IPP B_PYS-i3h-2.pdb	-101.65	-92.15	-9.5	0
cav2IPP B_PYS-i3i-1.pdb	-95.03	-87.46	-7.56	0
cav2IPP B_PYS-i4a-2.pdb	-97.04	-86.28	-10.76	0
cav2IPP B_PYS-i4b-2.pdb	-97.74	-84.14	-13.59	0
cav2IPP B_PYS-i4c-1.pdb	-94.45	-83.65	-10.79	0
cav2IPP B_PYS-i4d-0.pdb	-94.84	-83.90	-10.92	0
cav2IPP B_PYS-i4e-2.pdb	-98.95	-88.34	-10.60	0
cav2IPP B_PYS-i4f-1.pdb	-94.75	-83.99	-10.76	0
cav2IPP B_PYS-i4g-0.pdb	-97.51	-83.47	-14.03	0
cav2IPP B_PYS-i4h-0.pdb	-94.94	-85.29	-9.65	0
cav2IPP B_PYS-i4i-1.pdb	-88.44	-78.22	-10.22	0
cav2IPP B_PYS-BANA-2.pdb	-124.91	-85.51	-35.24	-4.15
cav2IPP B_PYS-leupeptin-2.pdb	-119.77	-91.77	-28.00	0

the results are one of the docking experiments run using igemdock under drug screening settings. the ligands were prepared in marvin sketch and saved as mdl mol file. the active site was extracted from the structure of cathepsin b retrieved from protein data bank (http://www.rcsb.org/) as cav2ipp b_pys.pdb.

Table-5: Docking studies showing decrease in different energies of cathepsin H in presence of different 4'-phenylchalcones and their pyrazolines derivatives

#Ligand	Total Energy (kcal/mol)	VDW	HBond	Elec
cav8PCH H_NAG-ic1a-2.pdb	-81.56	-72.77	-8.79	0
cav8PCH H_NAG-ic1b-1.pdb	-83.40	-75.13	-7.77	-0.49
cav8PCH H_NAG-ic1c-0.pdb	-74.38	-67.38	-7.00	0
cav8PCH H_NAG-ic1d-1.pdb	-80.50	-72.07	-8.42	0

cav8PCH H_NAG-ic1e-1.pdb	-81.31	-74.31	-7.0	0
cav8PCH H_NAG-ic1f-0.pdb	-81.03	-71.38	-9.65	0
cav8PCH H_NAG-ic1g-2.pdb	-89.72	-71.66	-17.22	-0.83
cav8PCH H_NAG-ic1h-2.pdb	-87.98	-79.85	-8.13	0
cav8PCH H_NAG-ic1i-2.pdb	-76.40	-66.94	-9.45	0
cav8PCH H_NAG-i2a-1.pdb	-86.66	-77.16	-9.5	0
cav8PCH H_NAG-i2b-1.pdb	-94.98	-73.03	-21.57	-0.37
cav8PCH H_NAG-i2c-1.pdb	-84.23	-74.75	-9.48	0
cav8PCH H_NAG-i2d-1.pdb	-81.93	-68.45	-13.48	0
cav8PCH H_NAG-i2e-1.pdb	-84.11	-65.51	-18.59	0
cav8PCH H_NAG-i2f-2.pdb	-88.30	-65.35	-22.95	0
cav8PCH H_NAG-i2g-2.pdb	-95.10	-75.22	-19.56	-0.31
cav8PCH H_NAG-i2h-2.pdb	-89.34	-79.84	-9.5	0
cav8PCH H_NAG-i2i-2.pdb	-81.92	-68.45	-13.47	0
cav8PCH H_NAG-i3a-0.pdb	-84.68	-78.80	-5.88	0
cav8PCH H_NAG-i3b-0.pdb	-94.59	-71.50	-22.20	-0.88
cav8PCH H_NAG-i3c-1.pdb	-83.40	-79.90	-3.5	0
cav8PCH H_NAG-i3d-1.pdb	-85.26	-81.65	-3.61	0
cav8PCH H_NAG-i3e-1.pdb	-92.05	-92.05	0	0
cav8PCH H_NAG-i3f-2.pdb	-91.06	-80.70	-10.35	0
cav8PCH H_NAG-i3g-1.pdb	-103.96	-91.03	-12.92	0
cav8PCH H_NAG-i3h-0.pdb	-87.89	-74.02	-13.87	0
cav8PCH H_NAG-i3i-1.pdb	-83.87	-83.87	0	0
cav8PCH H_NAG-i4a-1.pdb	-78.13	-62.25	-15.88	0
cav8PCH H_NAG-i4b-1.pdb	-86.41	-66.17	-20.23	0
cav8PCH H_NAG-i4c-0.pdb	-81.94	-71.44	-10.50	0
cav8PCH H_NAG-i4d-0.pdb	-83.12	-72.92	-10.19	0
cav8PCH H_NAG-i4e-1.pdb	-84.94	-78.11	-6.83	0
cav8PCH H_NAG-i4f-2.pdb	-87.79	-77.29	-10.5	0
cav8PCH H_NAG-i4g-0.pdb	-98.54	-71.57	-26.63	-0.33
cav8PCH H_NAG-i4h-0.pdb	-81.96	-66.87	-15.08	0
cav8PCH H_NAG-i4h-0.pdb	-84.58	-74.49	-10.08	0
cav8PCH H_NAG-leu bna-2.pdb	-79.13	-65.22	-13.90	0
cav8PCH H_NAG-leuCH2Cl-0.pdb	-59.99	-43.49	-16.5	0

the results are one of the docking experiments run using igemdock under drug screening settings. the ligands were prepared in marvin sketch and saved as mdl mol file. the active site was extracted from the structure of cathepsin h retrieved from protein data bank (http://www.rcsb.org/) as cav8pch h_nag.pdb.

Table-6: Docking studies showing decrease in different energies of cathepsin L in presence of different 4'-phenylchalcones and their pyrazolines derivatives

#Ligand	Total Energy (kcal/mol)	VDW	HBond	Elec
cav3BC3 L_CSW-i1a-1.pdb	-95.49	-95.49	0	0
cav3BC3 L_CSW-i1b-2.pdb	-88.05	-81.32	-6.72	0
cav3BC3 L_CSW-i1c-2.pdb	-93.42	-93.42	0	0
cav3BC3 L_CSW-i1d-2.pdb	-93.22	-93.22	0	0
cav3BC3 L_CSW-i1e-2.pdb	-92.47	-85.47	-7	0
cav3BC3 L_CSW-i1f-2.pdb	-95.81	-95.81	0	0
cav3BC3 L_CSW-i1g-1.pdb	-94.33	-94.33	0	0
cav3BC3 L_CSW-i1h-1.pdb	-101.48	-97.98	-3.5	0
cav3BC3 L_CSW-i1i-1.pdb	-92.26	-92.26	0	0
cav3BC3 L_CSW-i2a-0.pdb	-106.21	-102.71	-3.5	0
cav3BC3 L_CSW-i2b-2.pdb	-105.40	-101.90	-3.5	0
cav3BC3 L_CSW-i2c-2.pdb	-99.30	-95.80	-3.5	0
cav3BC3 L_CSW-i2d-1.pdb	-102.84	-99.34	-3.5	0
cav3BC3 L_CSW-i2e-1.pdb	-103.20	-100.67	-2.53	0
cav3BC3 L_CSW-i2f-2.pdb	-105.22	-101.72	-3.5	0
cav3BC3 L_CSW-i2g-2.pdb	-110.50	-94.54	-16.64	0.68
cav3BC3 L_CSW-i2h-1.pdb	-106.09	-102.59	-3.5	0
cav3BC3 L_CSW-i2i-0.pdb	-91.34	-91.34	0	0
cav3BC3 L_CSW-i3a-0.pdb	-108.26	-108.26	0	0
cav3BC3 L_CSW-i3b-1.pdb	-105.55	-105.55	0	0
cav3BC3 L_CSW-i3c-1.pdb	-107.17	-98.73	-8.43	0
cav3BC3 L_CSW-i3d-0.pdb	-105.35	-105.35	0	0
cav3BC3 L_CSW-i3e-2.pdb	-115.61	-107.41	-8.19	0
cav3BC3 L_CSW-i3f-1.pdb	-110.72	-102.24	-8.47	0
cav3BC3 L_CSW-i3g-2.pdb	-109.91	-103.15	-6.76	0
cav3BC3 L_CSW-i3h-0.pdb	-104.90	-102.27	-2.62	0
cav3BC3 L_CSW-i3i-0.pdb	-99.83	-96.33	-3.5	0

cav3BC3 L_CSW-i4a-1.pdb	-98.33	-83.78	-14.54	0
cav3BC3 L_CSW-i4b-0.pdb	-103.14	-80.63	-23.32	0.81
cav3BC3 L_CSW-i4c-1.pdb	-94.09	-87.09	-7	0
cav3BC3 L_CSW-i4d-1.pdb	-94.29	-94.29	0	0
cav3BC3 L_CSW-i4e-0.pdb	-97.25	-97.25	0	0
cav3BC3 L_CSW-i4f-0.pdb	-102.66	-92.50	-10.16	0
cav3BC3 L_CSW-i4g-2.pdb	-106.17	-93.35	-13.39	0.57
cav3BC3 L_CSW-i4h-1.pdb	-98.69	-85.32	-13.36	0
cav3BC3 L_CSW-i4i-0.pdb	-105.87	-102.37	-3.5	0
cav3BC3 L_CSW-leupeptin-2.pdb	-116.8	-91.45	-25.37	0
cav3BC3 L_CSW-Z-FR-BNA-1.pdb	-130.74	-115.02	-15.72	0

the results are one of the docking experiments run using igemdock under drug screening settings. the ligands were prepared in marvin sketch and saved as mdl mol file. the active site was extracted from the structure of cathepsinL retrieved from protein data bank (http://www.rcsb.org/) as cav3BC3 L_CSW.pdb.