# TABLE OF CONTENTS

Information	Page
Synthetic scheme for the synthesis of compound ( <b>3a&amp;3b</b> )	S-3
6-Bromo-2-cyclopropyl-4H-benzo[d][1,3]oxazin-4-one	S-3
6-Chloro-2-cyclopropyl-4H-benzo[d][1,3]oxazin-4-one	S-3
6-Bromo-2-cyclopropyl-3-(pyridin-3-ylmethyl) quinazolin-4(3H)-one ( <b>3a</b> )	S-4
6-Chloro-2-cyclopropyl-3-(pyridin-3-ylmethyl) quinazolin-4(3H)-one ( <b>3b</b> )	S-4
References	S-5
Table 1. Comparison of the rate of formation of 4a	S-6
Figure 1. Comparison of the rate of formation of 4a	S-6
Figure 2a. Insilico Studies-Sequence alignment	S-7
Figure 2b. Insilico Studies-Sequence alignment	S-7
Figure 2c. Insilico Studies-Sequence alignment	S-8
Fig 3. ELISA generated Optical Density (OD) Values	S-8
<b>Fig 4.</b> Screen shot of Calculations of IC50 values in Excel sheet and Screen shot of AGH 96 well pate	S-9
Table 2. Table 2. Physicochemical properties, Lipinski properties, ADMET properties   calculated for selected compounds	S-9
<b>Fig 4.</b> The predicted binding mode of 4f and \$0 to show the pi-pi interaction with the arometic residue of the active site	S-9
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 6-Bromo-2-cyclopropyl-4H-benzo[d][1,3]oxazin-4-one	S-10
<sup>(2a)</sup> <sup>1</sup> H and <sup>13</sup> C NMR spectra of 6-Chloro-2-cyclopropyl-4H-benzo[d][1,3]oxazin-4-one	S-11
<sup>(2b)</sup> <sup>1</sup> H and <sup>13</sup> C NMR spectra of 6-Bromo-2-cyclopropyl-3-(pyridin-3-ylmethyl) quinazolin- 4(3H)-one (3a)	S-12
<sup>-1</sup> H and <sup>13</sup> C NMR spectra of 6-Chloro-2-cyclopropyl-3-(pyridin-3-ylmethyl) quinazolin- 4(3H)-one ( <b>3b</b> )	S-13
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 2-cyclopropyl-6-phenyl-3-(pyridin-3-ylmethyl)quinazolin- 4(3H)-one ( <b>4a</b> )	S-14
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 2-cyclopropyl-6-(2-methoxyphenyl)-3-(pyridin-3- ylmethyl)quinazolin-4(3H)-one ( <b>4b</b> )	S-15
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 2-cyclopropyl-6-(3,4-dimethylphenyl)-3-(pyridin-3- ylmethyl)-quinazolin-4(3H)-one ( <b>4c</b> )	S-16
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 6-(2-acetylphenyl)-2-cyclopropyl-3-(pyridin-3-ylmethyl) quinazolin-4(3H)-one ( <b>4d</b> )	S-17
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 2-cyclopropyl-6-(3-fluoro-4-methylphenyl)-3-(pyridin-3- ylmethyl)quinazolin-4(3H)-one ( <b>4e</b> )	S-18
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 2-cyclopropyl-6-(2,6-dichlorophenyl)-3-(pyridin-3- ylmethyl)quinazolin-4(3H)-one ( <b>4f</b> )	S-19
<sup>1</sup> H and <sup>13</sup> C NMR spectra of Methyl-4-(2-cyclopropyl-4-oxo-3-(pyridin-3-ylmethyl)- 3.4-dihydroquinazolin-6-yl)benzoate ( <b>4</b> g)	S-20
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 4-[2-cyclopropyl-4-oxo-3-(pyridin-3-ylmethyl)-3,4- dihydroquinazolin-6-yllbenzonitrile ( <b>4</b> h)	S-21
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 2-cyclopropyl-6-(3-nitrophenyl)-3-(pyridin-3-	S-22

ylmethyl)quinazolin-4(3H)-one ( <b>4i</b> )	
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 2-cyclopropyl-6-(4-(dimethylamino)phenyl)-3-(pyridin-3-	S-23
ylmethyl)quinazolin-4(3H)-one ( <b>4j</b> )	
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 6-(3,5-bis(trifluoromethyl)phenyl)-2-cyclopropyl-3-	S-24
(pyridin-3-ylmethyl)quinazolin-4(3H)-one (4k)	
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 2-cyclopropyl-6-(4-(methylsulfonyl)phenyl)-3-(pyridin-3-	S-25
ylmethyl)quinazolin-4(3H)-one (4l)	
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 2-cyclopropyl-6-(2,4-dihydroxyphenyl)-3-(pyridin-3-	S-26
ylmethyl)quinazolin-4(3H)-one ( <b>4m</b> )	
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 2-cyclopropyl-6-(3,4-dihydroxyphenyl)-3-(pyridin-3-	S-27
ylmethyl)quinazolin-4(3H)-one ( <b>4n</b> )	
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 2-cyclopropyl-3-(pyridin-3-ylmethyl)-6-(2,3,4-	S-28
trihydroxyphenyl) quinazolin-4(3H)-one ( <b>40</b> )	
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 2-cyclopropyl-6-(naphthalen-1-yl)-3-(pyridin-3-ylmethyl)	S-29
quinazolin-4(3H)-one: ( <b>4p</b> )	
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 2-cyclopropyl-3-(pyridin-3-ylmethyl)-6-(pyridin-4-	<b>S-30</b>
yl)quinazolin-4(3H)-one ( <b>4q</b> )	
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 2-cyclopropyl-6-(1H-indol-6-yl)-3-(pyridin-3-	S-31
ylmethyl)quinazolin-4(3H)-one ( <b>4r</b> )	
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 6-(benzofuran-2-yl)-2-cyclopropyl-3-(pyridin-3-	S-32
ylmethyl)quinazolin-4(3H)-one ( <b>4</b> s)	
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 2-cyclopropyl-3-(pyridin-3-ylmethyl)-6-(thiophen-3-	S-33
yl)quinazolin-4(3H)-one ( <b>4</b> t)	
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 2-cyclopropyl-6-(3,5-dimethyl-1H-pyrazol-4-yl)-3-	S-34
(pyridin-3-ylmethyl)quinazolin-4(3H)-one ( <b>4u</b> )	
<sup>1</sup> H and <sup>13</sup> C NMR spectra 2-cyclopropyl-6-(3,5-dimethylisoxazol-4-yl)-3-(pyridin-3-	S-35
ylmethyl)quinazolin-4(3H)-one ( <b>4</b> v)	
<sup>1</sup> H and <sup>13</sup> C NMR spectra 2,6-dicyclopropyl-3-(pyridin-3-ylmethyl)quinazolin-4(3H)-	S-36
one( <b>4</b> w)	
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 2-cyclopropyl-6-isobutyl-3-(pyridin-3-	S-37
ylmethyl)quinazolin-4(3H)-one: ( <b>4x</b> )	
<sup>1</sup> H and <sup>13</sup> C NMR spectra of 2-cyclopropyl-6-methyl-3-(pyridin-3-ylmethyl)quinazolin-	S-38
4(3H)-one ( <b>4</b> y)	
Competitive reaction mixture LCMS results	S-39

**Scheme 1:** Synthetic scheme for the synthesis 6-Bromo and chloro-2-cyclopropyl-3-(pyridyl-3-ylmethyl) quinazolin-4(3*H*)-ones (**3a & 3b**)



Preparation of 6-bromo-2-cyclopropyl-4H-benzo[d][1,3]oxazin-4-one (2a):



A solution of cyclopropane carbonyl chloride (1 g, 4.62mmol) was added to a stirred solution of 2-amino-5-bromobenzoic acid (1 g, 4.62 mmol) in 2, 6-Lutidine (10 V) at 0 °C for 30 min, reaction mixture was allowed to rt and maintained 2h. Reaction mixture was poured in to ice cold water and filtered the solid, washed with water. Crude compound was used for next step without any further purification. Yield (60%, 0.73 g). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.27 (d, *J* = 2.1 Hz, 1H), 7.83 (dd, *J* = 8.2, 2.4 Hz, 1 H), 7.37 (d, *J* = 9.0 Hz, 1 H), 1.97-1.90 (m, 1H), 1.32-1.26 (m, 2H), 1.15-1.08 (m, 2H). <sup>13</sup>C NMR (75 MHz CDCl<sub>3</sub>):  $\delta$  = 164.6, 158.3, 145.7, 139.4, 130.7, 127.7, 120.3, 118.0, 14.3, 9.6.

## Preparation of 6-chloro-2-cyclopropyl-4H-benzo[d][1,3]oxazin-4-one (2b):



A solution of cyclopropane carbonyl chloride (1 g, 4.62mmol) was added to a stirred solution of 2-amino-5-chlorobenzoic acid (1 g, 4.62 mmol) in 2, 6-lutidine (10 V) at 0  $^{\circ}$ C for 30 min. Reaction mixture was allowed to rt and maintained for 2h. Reaction mixture was poured in to ice

cold water and filtered the solid, washed with water. Crude compound was used for next step without any further purification. Yield (60%, 0.73 g). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.11 (d, *J* = 2.0 Hz, 1H), 7.70 (dd, *J* = 8.4, 2.8 Hz, 1H), 7.45 (d, *J* = 9.0 Hz, 1H), 1.98-1.92 (m, 1H), 1.30-1.24 (m, 2H), 1.14 -1.11 (m, 2H). <sup>13</sup>C NMR (75 MHz CDCl<sub>3</sub>):  $\delta$  = 164.5, 158.4, 145.3, 136.6, 132.8, 127.6, 117.7, 14.3, 9.6.

#### Preparation of 6-bromo-2-cyclopropyl-3-(pyridin-3-ylmethyl) quinazolin-4(3H)-one (3a):



Pyridin-3-ylmethanamine (0.6 g, 5.63 mmol) was added to a solution of 6-bromo-2-cyclopropyl-3-(pyridin-3-ylmethyl) quinazolin-4(3*H*)-one (1g, 3.75 mmol) in acetic acid( 20 V), reaction mixture was heated to reflux for 2 h. After completion of the reaction, reaction mixture was cooled to rt, the mixture was poured in to ice cold water and filter the solid. The resulting solid was applied to a silica gel column, packed in 20% EtOAc in *n*-hexane. Sequential elution with 20% EtOAc in *n*-hexane and 50% EtOAc in *n*-hexane gave 6-bromo-2-cyclopropyl-3-(pyridin-3ylmethyl)quinazolin-4(3*H*)-one (**3a**) as a white solid. Yield (1.07 g, 80%). <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>):  $\delta$  = 8.58 (s, 1 H), 8.49 (d, *J* = 4.8 Hz, 1 H), 8.20 (d, *J* = 1.6 Hz, 1 H), 7.93 (dd, *J* = 2.4, 2.4 Hz, 1 H), 7.64 (d, *J* = 8.0 Hz), 7.50 (d, *J* = 8.8 Hz, 1 H), 7.39-7.34 (m, 1 H), 5.58 (s, 2 H), 2.19-2.13 (m, 1 H), 1.10-1.06 (m, 2 H), 0.97-0.92 (m, 2 H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$ 160.5, 158.7, 148.5, 148.2, 146.0, 137.2, 134.4, 132.2, 129.0, 128.4, 123.6, 121.3, 118.2, 44.0, 13.9, 9.4.

### Preparation of 6-chloro-2-cyclopropyl-3-(pyridin-3-ylmethyl) quinazolin-4(3H)-one (3b):



Pyridin-3-ylmethanamine (0.6 g, 5.63 mmol) was added to a solution of 6-chloro-2-cyclopropyl-3-(pyridin-3-ylmethyl) quinazolin-4(3H)-one (1g, 3.75 mmol) in acetic acid (20 V), reaction mixture was heated to reflux for 2 h. After completion of the reaction, reaction mixture was cooled to rt. The mixtures was poured in to ice cold water and filter the solid. The resulting solid was applied to a silica gel column packed in 20% EtOAc in n-hexane. Sequential elution with 20% EtOAc in n-hexane and 50% EtOAc in n-hexane gave 1.1 g of 6-bromo-2-cyclopropyl-3-(pyridin-3-ylmethyl)quinazolin-4(*3H*)-one as a white solid. Yield (1.07 g, 80%). <sup>1</sup>H NMR (400MHz, DMSO-d<sub>6</sub>):  $\delta$  = 8.58 (s, 1H), 8.50 (d, *J* = 3.6 Hz, 1 H), 8.06 (s, 1H), 7.82 (d, *J* =, 8.8 Hz, 1 H), 7.66 (d, *J* = 8.0 Hz 1 H), 7.58 (d, *J* = 8.8 Hz, 1 H), 7.37 (dd, *J* = 7.2, 4.8 Hz, 1H), 5.58 (s, 2H), 2.18-2.16 (m, 1H), 1.08-1.03 (m, 2H), 0.96-0.94 (m, 2H). <sup>13</sup>C NMR (75 MH<sub>Z</sub> CDCl<sub>3</sub>):  $\delta$  = 160.5, 158.7, 148.5, 148.2, 146.0, 137.2, 134.4, 132.2, 129.0, 128.4, 123.6, 121.3, 118.2, 44.0, 13.9, 9.4.

### References

 a) J.-F. Liu, J. Lee, A. M. Dalton, G. Bi, L. Yu, C. M. Baldino, E. McElory and M. Brown, *Tetrahedron Lett.*, 2005, 46, 1241; (b) C. Carolyn, J. D. Brackett and D. O. Bloch, *Pharmacotherapy* 2000, 20, 229; (c) P. M. Chandrika, T. Yakaiah, A. R. R. Rao, B. Narsaiah, N. C. Reddy, V. Sridhar and J. V. Rao, *Eur. J. Med. Chem.*, 2008, 43, 846; (d) P. M. Chandrika, T. Yakaiah, B. Narsaiah, V. Sridhar, G. Venugopal, J. V. Rao, K. P. Kumar, U. S. N. Murthy and A. R. R. Rao, *Indian J. Chem.*, 2009, 48, 840; (e) G. Rabilloud and B. Sillion, *J. Heterocyclic. Chem.*, 1980, 17, 1065-1068.

	1h	2h	3h	4h	8h	16h	24h
1mol%	10	15	19	24	33	45	45
2mol%	27	36	38	42	56	66	67
5mol%	69	76	80	81	84	87	88
10mol%	93	95	96	97	97	96	96
20mol%	94	96	98	98	98	99	98
30mol%	94	94	94	95	97	96	95

**Table 1** Comparison of the rate of formation of 4a in % yield with different mol% of precatalyst loading on 3a with PhB(OH)<sub>2</sub>

**Fig. 1** Comparison of the rate of formation of 4a with different mol% of pre-catalyst loading on 3a with PhB(OH)<sub>2</sub> at 80  $^{\circ}$ C( formation of 4a in percentages, determined by LCMS). K<sub>3</sub>PO<sub>4</sub> as base and 1,4-dioxane as solvent.



Fig. 2a Insilico studies-Sequence Alignment

2QIY_A   POBID   CHAIN   SEQUENCE 21 AT AL DORID   CHAIN   SEQUENCE	SAFC PUVN	8	Accelerating head
sp  P10253  LYAG_HUMAN	M3VFRPPCSHFLLAVCALVSLATAALLGHILLHDFLLVPFELSGSSFVLE ****::	50	
2QIY_A   PDBID   CHAIN   SEQUENCE	ELERINCIPDQPPTK	23	
3L4T_A PDBID CHAIN SEQUENCE sp P10253 LYAG_HUMAN	ELERINCIPDQPPTK ETHPAHQQGASRPGPFDAQAHPGRPRAVYTQCDVPPNSRFDCAPDKAITQ * . *::* *: *: *:	23 100	
2QIY_A   PDBID   CHAIN   SEQUENCE	ATCDQR6CCWNPQGAV5-VPWCYYSENHSYHVEGNLVNTNAGFTA	67	
3L4T_A PDBID CHAIN 3EQUENCE sp P10253 LYAG_HUMAN	ATCDQRGCCWNPQGAV3-VPWCYY3ENHI3YHVEGNLVNTNAGFTA EQCEARGCCYIPAKQGLQGAQNGQPWCFFPPSYPSYKLENLSSSENGYTA *: ****: * *** ***:: ** .:: ** .:: **	67 150	
2017_ALPOBIDICHAINISEOUENCE	RLKNLPSSPVFGSNVDNVLLTAEYOTSNEFHFKLTDOTNNRFEVPHEHVO	117	
3L4T_A PDBID CHAIN SEQUENCE cp P10253 LYAG_HUMAN	PLENLPSSPVFGSNVDNVLLTAEYQTSNRFHFKLTDQTNNRFEYPHEHVQ TLT-RTPTFFPRDILTLRLDVMMETENRLHFTIKDPANRRYEYPLETPH ***.:*.:*.:*.:*.:*.:*.:*.:*.*:*.*	117 199	
2QIY_A   PDBID   CHAIN   SEQUENCE	SFSGNALASLTYQVEISRQPFSIKVTRRSNNRVLFDSSIGPLLFADQFLQ	167	
3L4T_A PDBID CHAIN SEQUENCE sp P10253 LVAG_HUMAN	SFSGNAAASLTYQVEISRQ?FSIKVTFRSNNRVLFDSSIGPLLFADQFLQ VHSRAPSPLYSVEFSEE?FGVIVRRQLDGRVLLNTTVAPLFFADQFLQ .* 7.5 *.**:*.:**: * *: :.***::::::.**	167 247	
2QIY_A   PDBID   CHAIN   SEQUENCE	L3TRLPSTNVYGLGEHVHQQYRHDMN0KTWP1FNRDTTPNGNGTNLYGAQ	217	
3L4T_A PDBID CHAIN SEQUENCE sp P10253 LYAG_HUMAN	LSTRLPSTWVYGLGEHVHQQYRHDMNWKTWPI/NRDTTPNGNGTNLYGAQ LSTSLPSQYITGLAEHLSPLMLSTS-WTRITLUNRDLAPTP-GANLYGSH *** *** : **.**: *::*** :*. *:****:	217 295	
2QIY_A   PDBID   CHAIN   SEQUENCE	TFFLCLEDASGLSFGVFLMNSNAMEVVLQPAPAITYRTIGGILDFYVFLG	267	
3L4T_A PDBID CHAIN 3EQUENCE sp P10253 LYAG HUMAN	TFFLCLEDASGLSFGVFLMDSNAMEVVLQPAPAITYRTIGGILDFYVFLG PFYLALEDG-GSAHGVFLLDSNAMDVVLQPSPALSWRSTGGILDVYIFLG	267 344	

Fig. 2b Insilico studies-Sequence Alignment







Fig 3. ELISA generated Optical Density (OD) Values

	1	2	3	4	5	6	7	8	9	10	11	12		1	2	3	4	5	6	7	8	9	10	11	12
A 0	h_0001 1/1 :1 .116	12 Un_0001 2 1:1 0.189	/12 Un_0001 3/1 1:1 0.188	2 Un_0001 4/1 1:1 0:144	2 Un_0001 5/1: 1:1 0.171	2 Un_0001 6/1 1:1 0.069	2 Un_0001 7/13 1:1 0.099	2 Un_0001 8/12 1:1 0.076	E Un_0001 9/12 1:1 0.075	Un_0001 10/1 1:1 0.095	Un_0001 11/ 1:1 0.263	1: Un_0001 12/12 1:1 0:271	A	Jn_0001 1/1 1:1 1:193	2 Un_0001 2/1 1:1 0.861	2 Un_0001 3/1 1:1 0:194	12 Un_0001 4/1 1:1 0,184	2 Un_0001 5/1: 1:1 0.107	2 Un_0001 6/13 1:1 0.170	Un_0001 7/12 1:1 0.410	2 Un_0001 8/13 1:1 0.667	2 Un_0001 9/13 1:1 1.082	Un_0001 10/ 1:1 1.674	1: Uh_0001 11/ 1:1 0.072	11: Un_0001 11 1:1 1.610
U 1 0	h_0002 1/1 :1 :102	12 Un_0002 2 1:1 0.188	/12 Un_0002 3/1 1:1 0.187	12 Un_0002 4/1: 1:1 0:140	2 Un_0002 6/1: 1:1 0.168	2 Un_0002 6/1 1:1 0.065	2 Un_0002 7/12 1:1 0.099	2 Un_0002 8/12 1:1 0.083	Un_0002 9/12 1:1 0.090	Un_0002 10/1 1:1 0:105	Un_0002 11/ 1:1 0.505	1: Un_0002 12/12 1:1 0.515	B	Jn_0002 1/1 1:1 1:214	2 Un_0002 2/1 1:1 0.225	2 Un_0002 3/1 1:1 0:254	12 Un_0002 4/1 1:1 0:223	2 Un_0002 5/1 1:1 0.137	2 Un_0002 6/12 1:1 0:284	Un_8002 7/12 1:1 0.424	2 Un_0002 8/13 1:1 0.840	2 Un_0002 9/1; 1:1 0.990	Un_8882 187 1:1 1.573	1: Un_0002 11/ 1:1 0.051	n: Un_0002 1 1:1 0.062
U 1 0	n_0003 1/1 :1 :269	12 Un_0003 2 1:1 0:558	/12 Un_0003 3/1 1:1 0.232	2 Un_0003 4/1 1:1 0:277	2 Un_0003 5/1: 1:1 0.131	2 Un_0003 6/1 1:1 0:152	2 Un_0003 7/13 1:1 0.204	2 Un_0003 8/12 1;1 0.092	: Un_0003 9/12 1:1 0.089	: Un_0003 10/1 1:1 0.078	: Un_0003 11/ 1:1 0.674	1: Un_0003 12/12 1:1 0.661	c	Jn_0003 1/1 1:1 1.061	2 Un_0003 2/1 1:1 0.093	2 Un_0003 3/1 1:1 0:102	12 Un_0003 4/1 1:1 0.095	2 Un_0003 5/1: 1:1 0.112	2 Uh_0003 6/12 1:1 0.060	Un_0003 7/12 1:1 0.059	2 Un_0003 8/13 1:1 0.105	2 Uh_0000 9/1: 1:1 0.145	Un_8003 10/ 1:1 0.094	1: Un_0003 11/ 1:1 0.056	rt: Un_0800 1 1:1 0:061
0	n_0004 1/1 :1 :336	12 Un_0004 2 1:1 0.540	/12 Un_8004 3/1 1:1 0.231	2 Un_0004 4/1 1:1 0.212	2 Un_0004 5/1: 1:1 0.122	2 Un_0004 6/1 1:1 0.146	2 Un_0004 7/1: 1:1 0.253	2 Uh_0004 8/12 1:1 0.091	2 Un_0004 9/12 1:1 0.076	1 Un_0004 10/1 1:1 0.077	Un_0004 11/ 1:1 0.680	1: Un_0004 12/12 1:1 0.652	D	Jn_0004 1/1 1:1 1.056	2 Un_0004 2/1 1:1 0.093	2 Un_0004 3/1 1:1 0.111	12 Un_0004 4/1 1:5 0.121	2 Un_0004 6/1: 1:1 0.118	2 Un_0004 6/12 1:1 0.055	Un_0004 7/12 1:1 0:056	2 Un_0004 8/13 1:1 0.084	2 Un_0004 9/1: 1:1 0.070	: Un_0004 10/ 1:1 0.131	1: Un_0004 11/ 1:1 0.084	1: U6_0004 1:1 0.066
U 1 9	h_0005 1/1 :1 .064	12 Un_0005 2 1:1 0.132	/12_Un_0006_3/1 1:1 0.068	2 Un_0005 4/1 1:1 0.096	2 Un_0005 5/1: 1:1 0.078	2 Un_0005 6/1 1:1 0.061	2 Un_0005 7/1: 1:1 0.093	2 Uh_0005 8/12 1:1 0.086	2 Un_0005 9/12 1:1 0.081	: Un_0005 10/1 1:1 0.091	Un_0005 11/ 1:1 0.227	1: Un_0005 12/12 1:1 0.219	E	Jn_0006 1/1 [:1 [.137	2 Un_0006 2/1 1:1 0.122	2 Un_0006 3/1 1:1 0.171	12 Un_0005 4/1 1:1 0:097	2 Un_0005 5/1: 1:1 0.079	2 Un_0005 6/12 1:1 0.263	Un_0005 7/11 1:1 0.309	2 Un_0005 8/13 1:1 0.402	2 Uh_0005 9/1: 1:1 0 486	: Un_0005 10/ 1:1 0.309	1:1 1:1 0.037	n: Un_0005 1:1 0.040
0	h_0006 1/1 :1 .073	12 Un_0006 2 1:1 0.132	/12 Un_0006 3/1 1:1 0.069	2 Un_0006 4/1: 1:1 0.075	2 Un_0006 5/1: 1:1 0.076	2 Un_0006 6/1 1:1 0.065	2 Un_0006 7/12 1:1 0.098	2 Un_0006 8/12 1:1 0.094	2 Un_0006 9/12 1:1 0.078	Un_0006 10/1 1:1 0.107	Un_0006 117 1:1 0.088	1: Un_0006 12/12 1:1 0.070	F	Jn_0008 1/1 1:1 1.084	2 Un_0006 2/1 1:1 0:104	2 Un_0006 3/1 1:1 0.115	12 Un_0006 4/1 1:1 0.147	2 Un_0006 6/1; 1:1 0.128	2 Un_0006 6/12 1:1 0:206	Un_0006 7/12 1:1 0.293	2 Un_0006 8/1: 1:1 0.471	2 Un_0006 9/13 1:1 0.361	Un_0006 10/ 1:1 0:392	1: Un_0006 11/ 1:1 0.046	71: Un_0008 1:1 0.041
10	h_0007 1/1 :1 :377	12 Un_0007 2 1:1 0.691	/12 Un_6007 3/1 1:1 1.019	2 Un_0007 4/1: 1:1 1.299	2 Un_0007 5/1: 1:1 0.850	2 Un_0007 6/1 1:1 0.162	2 Un_0007 7/12 1:1 0.341	2 Un_0007 8/12 1:1 0.272	Un_0007 9/12 1:1 0.162	1:1 0.126	Un_0007 117 1:1 0.079	1: Un_0007-12/12 1:1 0.107	G	Jn_0007 1/1 1:1 1:072	2 Uh_0007 2/1 1:1 0.082	2 Un_0007 3/1 1:1 8.140	12 Un_0007 4/1 1:1 0:106	2 Un_0007 6/1: 1:1 0.102	2 Un_0007 6/12 1:1 0.051	Un_0007 7/12 1:1 0.088	Un_0007 8/13 1:1 0.103	2 Un_0007 9/1: 1:1 0.113	: Un_0007 10/ 1:1 0.108	1: Un_0007 11/ 1:1 0.039	1: U6_0007 1:1 0.041
1 0	h_0008 1/1 :1 :359	12 Un_0008 2 1:1 0.704	/12 Un_0008 3/1 1:1 1.052	2 Un_0008 4/1: 1:1 1,239	2 Un_0008 5/1: 1:1 0.808	2 Un_0008 6/1 1:1 0.159	2 Un_0008 7/13 1:1 0.339	2 Un_0008 8/12 1:1 0.288	Un_0008 9/12 1:1 0.149	Un_0008 10/1 1:1 0.133	Un_0008 11/ 1:1 0.090	1: Un_0008 12/12 1:1 0.067	H O	Jn_0009 1/1 1:1 1:094	2 Un_0008 2/1 1:1 0.088	2 Un_0008 3/1 1:1 0.059	12 Un_0008 4/1 1:1 0:051	2 Un_0008 5/1: 1:1 0.055	2 Un_0008 6/15 1:1 0.043	Un_0008 7/13 1:1 0.087	Un_0008 8/12 1:1 0.049	2 Un_0008 9/1: 1:1 0.062	Un_0008 10/ 1:1 0.055	1: Uh_0008 11/ 1:1 0.052	n: Un_0008 1:1 0.047



#### Fig 4. Screen shot of Calculations of IC50 values in Excel sheet and Screen shot of AGH 96 well pate

Table 2. Physicochemical properties, Lipinski properties, ADMET properties calculated for selected compounds

Name	PSA	HBA	NRB	NR	MW	HBD	ALogP	BBB	Abs	Sol	hERG pIC50
4q	58.45	4	4	5	354.40	0	2.59	2	0	-4.27	4.71
4u	74.24	4	4	5	371.44	1	2.62	2	0	-4.51	4.40
4x	45.56	3	5	4	333.43	0	3.88	1	0	-5.15	5.26
4w	45.56	3	4	5	317.38	0	3.05	1	0	-4.66	5.22
4y	45.56	3	3	4	291.35	0	2.71	1	0	-4.24	4.91
4s	58.70	3	4	6	393.44	0	4.34	1	0	-6.21	5.44
4r	61.35	3	4	6	392.45	1	4.04	1	0	-6.02	5.10
4t	73.80	3	4	5	359.44	0	3.41	1	0	-4.67	5.04
4a	45.56	3	4	5	353.42	0	3.74	1	0	-5.27	5.13
4p	32.67	2	4	6	402.49	0	5.80	0	0	-7.55	5.94

*Abbreviations:* PSA :Polar surface area; HBA :Num\_H\_Acceptors; NRB :Num\_RotatableBonds; NR :Num\_Rings;; MW :Molecular\_Weight; HBD :Num\_H\_Donors; ALogP :ALogP;

BBB :ADMET\_BBB\_Level (0 high to 2 Medium penetration); Abs :ADMET\_Absorption\_Level (0 = Good; 1 = Moderate; 2 = Low; 3 = Very low); Sol :ADMET\_Solubility (-8 low to -2 good ), hERG pIC50 values should be around 5.

Fig 5. The predicted binding mode of 4f and \$0 to show the pi-pi interaction with the aromatic residue of the active site



The active site of the glucosidase contains hydrophobic region surrounded by Trp530, Trp433, Trp293, Trp398, Phe442 amino acids. The binding mode of these compounds 4f, 4o also reveal that the hydrophobic groups were well tightly fixed in the hydrophobic region of the glucoside active site.





Analyst Sign:







Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry This journal is The Royal Society of Chemistry 2013





























Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry This journal is The Royal Society of Chemistry 2013



















Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry This journal is The Royal Society of Chemistry 2013











