Supporting Information for:-

Discovery of monocarbonyl curcumin hybrids as a novel class of human DNA ligase I inhibitors: In silico design, synthesis and biology

Dhanaraju Mandalapu,§,a Deependra Kumar Singh,§,b Sonal Gupta,ac Vishal M. Balaramnavar,b,1 Mohammad Shafiq,b Dibyendu Banerjee*,b,cd and Vishnu Lal Sharma*,a,cd

a Medicinal & Process Chemistry Division, b Molecular & Structural Biology Division, CSIR-Central Drug Research Institute (CSIR-CDRI), Jankipuram Extension, Sitapur Road, Lucknow 226031, c Department of Pharmaceutical Chemistry, Global Institute of Pharmaceutical Education and Research, Kashipur, Uttarakhand, India, 244713. d Academy of Scientific and Innovative Research (AcSIR), New Delhi-110001 (India).

* Corresponding authors: 1. Dr. Vishnu Lal Sharma, Medicinal and Process Chemistry Division, Tel.: 91-522-2772450; Ext. 4671; Fax: 91-522-2771941, E-mail: vl_sharma@cdri.res.in; vlscdri@gmail.com. 2. Molecular & Structural Biology Division, CSIR-Central Drug Research Institute (CSIR-CDRI), Jankipuram Extension, Sitapur Road, Lucknow 226031, Tel.: 91-522-2772450; Ext. 4443; Fax: 91-522-2771941; E-mail: d.banerjee@cdri.res.in; dibyendu25@hotmail.com.

§ Both authors contributed equally.

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### Table S1. The summaries of hypothesis run

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Direct hitmask indicates [1] or (0) not a training set molecule mapped every feature. Partial hit mask indicates whether [1] or (0) not a molecule mapped all but one feature. *Z; hydrophobic, A; hydrogen bond acceptor (HBA) and R; ring aromatic

### Table S2. The scoring functions from docking runs and fit values from generated pharmacophore model.

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$^{13}$C NMR Spectra of compound 14 (100 MHz, CDCl$_3$)
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\(^1^3^C\) NMR Spectra of compound 15\((100 \text{ MHz, CDCl}_3+\text{DMSO-}d_6)\)
$^1$H NMR Spectra of compound 16 (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of compound 16 (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of compound 17 (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of compound 17 (100 MHz, CDCl$_3$)
\( ^1H \) NMR Spectra of compound 18(400 MHz, CDCl\(_3\))

\( ^13C \) NMR Spectra of compound 18(100 MHz, CDCl\(_3\)+DMSO-\(d_6\))
$^1$H NMR Spectra of compound 19 (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of compound 19 (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of compound 20 (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of compound 20 (100 MHz, CDCl$_3$+DMSO-$d_6$)
$^1$H NMR Spectra of compound 21 (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of compound 21 (100 MHz, CDCl$_3$+DMSO-$d_6$)
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$^{1}$H NMR Spectra of compound 23 (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of compound 23 (100 MHz, CDCl$_3$)
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$^{13}$C NMR Spectra of compound 24 (100 MHz, DMSO-$d_6$)
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$^{13}$C NMR Spectra of compound 25 (100 MHz, CDCl$_3$)
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$^{13}$C NMR Spectra of compound 26 (100 MHz, CDCl$_3$+DMSO-$d_6$)
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$^{13}$C NMR Spectra of compound 27 (100 MHz, CDCl$_3$+DMSO-$d_6$)
$^1$H NMR Spectra of compound 28 (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of compound 28 (100 MHz, DMSO-$d_6$)
$^{1}H$ NMR Spectra of compound 29 (400 MHz, CDCl$_3$)

$^{13}C$ NMR Spectra of compound 29 (100 MHz, CDCl$_3$+DMSO-$d_6$)
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$^{13}$C NMR Spectra of compound 30 (100 MHz, CDCl$_3$+DMSO-$d_6$)
$^1$H NMR Spectra of compound 31 (400 MHz, CDCl$_3$)

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\(^1\)H NMR Spectra of compound 32 (400 MHz, CDCl\(_3\)+DMSO-\(d_6\))

\(^{13}\)C NMR Spectra of compound 32 (100 MHz, CDCl\(_3\)+DMSO-\(d_6\))
$^{1}$H NMR Spectra of compound 33 (400 MHz, CDCl$_3$+DMSO-$d_6$)

$^{13}$C NMR Spectra of compound 33 (100 MHz, DMSO-$d_6$)
$\text{H NMR Spectra of compound 34 (400 MHz, CDCl}_3$)

$\text{C NMR Spectra of compound 34 (100 MHz, DMSO-d}_6$)
$\text{H NMR Spectra of compound 35} (400 \text{ MHz, CDCl}_3+\text{DMSO}-d_6)$

$\text{C NMR Spectra of compound 35} (100 \text{ MHz, DMSO}-d_6)$
$^1$H NMR Spectra of compound 36 (400 MHz, CDCl$_3$+DMSO-$d_6$)

$^{13}$C NMR Spectra of compound 36 (100 MHz, DMSO-$d_6$)
$^1$H NMR Spectra of compound 37(400 MHz, DMSO-$d_6$)
H NMR Spectra of compound 38 (400 MHz, CDCl₃)

13C NMR Spectra of compound 38 (100 MHz, CDCl₃)
$^1$H NMR Spectra of compound 39 (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of compound 39 (100 MHz, CDCl$_3$+DMSO-$d_6$)
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$\textbf{1}^3\text{C} \text{ NMR Spectra of compound 40 (100 MHz, CDCl}_3 \text{)}$
$^1$H NMR Spectra of compound 41 (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of compound 41 (100 MHz, CDCl$_3$+DMSO-$d_6$)
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$^1$H NMR Spectra of compound 43 (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of compound 43 (100 MHz, CDCl$_3$)
¹H NMR Spectra of compound 44 (400 MHz, CDCl₃)

¹³C NMR Spectra of compound 44 (100 MHz, DMSO-d₆)
$^1$H NMR Spectra of compound 45 (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of compound 45 (100 MHz, CDCl$_3$+DMSO-$d_6$)
$^1$H NMR Spectra of compound 46 (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of compound 46 (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of compound 47 (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of compound 47 (100 MHz, CDCl$_3$)
H NMR Spectra of compound 48 (400 MHz, CDCl₃)

13C NMR Spectra of compound 48 (100 MHz, DMSO-d₆)
**H NMR Spectra of compound 49 (400 MHz, CDCl$_3$)**

**C NMR Spectra of compound 49 (100 MHz, CDCl$_3$+DMSO-$d_6$)**
DEPT-135 Spectra of compound 47 (100 MHz, CDCl$_3$)
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Exact Mass [M+H]^+: 461.1499

[4H+1] Exact mass = 461.1499
HRMS of compound 16

Chemical Formula: C_{29}H_{28}N_{2}O_{2}S
Exact Mass [M+H]: 453.2001

HRMS of compound 17

Chemical Formula: C_{29}H_{28}N_{2}O_{2}S
Exact Mass [M+H]: 453.2001
HRMS of compound 18

HRMS of compound 19
HRMS of compound 20

Chemical Formula: C_{23}H_{24}F_{2}N_{2}O_{2}S
Exact Mass [M+H]: 475.1656

HRMS of compound 21

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Exact Mass [M+H]: 467.2157

![HRMS Graph](image)

### HRMS of compound 23

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Chemical Formula: C<sub>30</sub>H<sub>30</sub>N<sub>2</sub>O<sub>5</sub>

Exact Mass [M+H]: 467.2157

![HRMS Graph](image)
HRMS of compound 24

Chemical Formula: C_{30}H_{29}N_{2}O_{5}S
Exact Mass [M+H]: 499.2055

HRMS of compound 25

Chemical Formula: C_{34}H_{38}N_{2}O_{5}S
Exact Mass [M+H]: 523.2763
### HRMS of compound 26

**Chemical Formula:** C_{26}H_{20}F_{2}N_{2}OS

**Exact Mass [M+H]:** 447.1343

![HRMS Diagram for Compound 26](image1)

### HRMS of compound 27

**Chemical Formula:** C_{26}H_{20}F_{2}N_{2}OS

**Exact Mass [M+H]:** 447.1343

![HRMS Diagram for Compound 27](image2)
HRMS of compound 28

Chemical Formula: C_{28}H_{26}N_{2}O_{3}S
Exact Mass [M+H]: 439.1844

HRMS of compound 30

Chemical Formula: C_{28}H_{26}N_{2}O_{3}S
Exact Mass [M+H]: 471.1742
HRMS of compound 31

Chemical Formula: \( \text{C}_{32}\text{H}_{34}\text{N}_{2}\text{O}_{5} \)
Exact Mass [M+H]: 495.2470

HRMS of compound 32

Chemical Formula: \( \text{C}_{27}\text{H}_{20}\text{F}_{2}\text{N}_{2}\text{O}_{2}\text{S} \)
Exact Mass [M+H]: 475.1292
HRMS of compound 33

Chemical Formula: C_{27}H_{26}F_{2}N_{2}O_{2}S
Exact Mass [M+H]: 475.1292

HRMS of compound 34

Chemical Formula: C_{29}H_{29}N_{2}O_{2}S
Exact Mass [M+H]: 467.1793
HRMS of compound 35

HRMS of compound 36
HRMS of compound 37

Chemical Formula: C_{37}H_{34}N_{2}O_{3}S
Exact Mass [M+H]: 523.2419

HRMS of compound 38

Chemical Formula: C_{28}H_{32}F_{2}N_{2}OS
Exact Mass [M+H]: 427.1656
HRMS of compound 39

Chemical Formula: C_{29}H_{36}F_{2}N_{2}O_{5}
Exact Mass [M+H]: 427.1656

HRMS of compound 40

Chemical Formula: C_{26}H_{26}N_{2}O_{5}
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HRMS of compound 41

Chemical Formula: C_{26}H_{35}N_{2}O_{5}S
Exact Mass [M+H]: 451.2055

HRMS of compound 42

Chemical Formula: C_{26}H_{35}N_{2}O_{5}S
Exact Mass [M+H]: 451.2055
HRMS of compound 43

Chemical Formula: C_{30}H_{30}N_{2}O_{5}S
Exact Mass [M+H]: 475.2763

HRMS of compound 45

Chemical Formula: C_{28}H_{26}F_{2}N_{2}O_{5}S
Exact Mass [M+H]: 471.1343
HRMS of compound 46

Chemical Formula: C_{30}H_{26}N_{2}O_{5}S
Exact Mass [M+H]: 463.1844

HRMS of compound 47

Chemical Formula: C_{30}H_{26}N_{2}O_{5}S
Exact Mass [M+H]: 463.1844
HRMS of compound 48

Chemical Formula: C_{30}H_{26}N_{2}O_{3}S

Exact Mass [M+H]: 495.1742

HRMS of compound 49

Chemical Formula: C_{34}H_{34}N_{2}O_{3}

Exact Mass [M+H]: 519.2467

\[(\n+1) = \text{Exact mass} 519.2470\]
**IC₅₀ calculation** - We have calculated the IC₅₀ value by the Graph Pad Prism software version 5.01. For the calculation of IC₅₀ values we have performed antiligase activity of compound 23 at 100, 50, 25, 12.5, and 6.25 µM concentrations whereas antiproliferative activity was performed at 50, 25, 12.5, 6.25 and 3.12 µM concentrations. At the different concentration of compound 23, percent of antiligase and antiproliferative activities were determined and IC₅₀ values were calculated by plotting the data log inhibitor vs. normalised response using Graph Pad Prism. The graphs have been shown in figure S2. We have found 24.9±1.8 µM (Figure S2A) and 8.7±1.9 µM (Figure S2B) IC₅₀ values for antiligase and antiproliferative activities of compound 23 respectively.

**Figure S2. Graphs for IC₅₀ calculation (A) for antiligase activity (B) for antiproliferative activity.**