Supplementary Information for

ORIGINAL ARTICLE

Discovery of N-aryl sulfonamide-quinazoline derivatives as anti-gastric cancer agents in vitro and in vivo via activating the Hippo signaling pathway

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In this work, compound 9i was designed and synthesized by SAR study of our reported tertiary amide derivatives compound 1 and compound 2. Therefore, we tested the influence of compound 9i on tubulin polymerization and AKT/mTOR and ERK pathways. As showed in Supporting Figure S1, compound 9i shows no strong influence on tubulin polymerization and P38, ERK, AKT, mTOR and Wnt pathways. Fortunately, we found compound 9i showed an obvious activation activity on hippo pathway. Therefore, we here reported N-sulfonamide-quinazoline derivatives as novel anti-gastric cancer agents via activating the Hippo signaling pathway \textit{in vitro} and \textit{in vivo}.

\textbf{Supporting Figure S1.} A. Activity of compound 9i on tubulin polymerization. Tubulin polymerization extracellular, concentrations of Paclitaxel, Colchicine and 9i were 3 μmol/L; Activity of compound 9i on P38, ERK, AKT, mTOR and Wnt pathways, cells were incubated with 20, 40 and 60 nM 9i for 48 hours.
- $^1$H, $^{13}$C-NMR and HRMS of Compound 6a

Figure S2. $^1$H NMR spectrum of compound 6a (400 MHz, DMSO-$d_6$)

Figure S3. $^{13}$C NMR spectrum of compound 6a (100 MHz, DMSO-$d_6$)
Figure S4. HRMS spectrum of compound 6a

- $^1$H, $^{13}$C-NMR and HRMS of Compound 6b

Figure S5. $^1$H NMR spectrum of compound 6b (400 MHz, DMSO-$d_6$)
Figure S6. $^{13}$C NMR spectrum of compound 6b (100 MHz, DMSO-$d_6$)

Figure S7. HRMS spectrum of compound 6b

- $^1$H, $^{13}$C-NMR and HRMS of Compound 6c

Figure S8. $^1$H NMR spectrum of compound 6c (400 MHz, DMSO-$d_6$)
Figure S9. $^{13}$C NMR spectrum of compound 6c (100 MHz, DMSO-$d_6$)

Figure S10. HRMS spectrum of compound 6c
- $^1$H, $^{13}$C-NMR and HRMS of Compound 6e

Figure S11. $^1$H NMR spectrum of compound 6e (400 MHz, DMSO-$d_6$)

Figure S12. $^{13}$C NMR spectrum of compound 6e (100 MHz, DMSO-$d_6$)
Figure S13. HRMS spectrum of compound 6e

- $^1$H, $^{13}$C-NMR and HRMS of Compound 6f

Figure S14. $^1$H NMR spectrum of compound 6f (400 MHz, DMSO-$d_6$)
Figure S15. $^{13}$C NMR spectrum of compound 6f (100 MHz, DMSO-$d_6$)

Figure S16. HRMS spectrum of compound 6f
- $^1$H, $^{13}$C-NMR and HRMS of Compound 6g

Figure S17. $^1$H NMR spectrum of compound 6g (400 MHz, DMSO-d$_6$)

Figure S18. $^{13}$C NMR spectrum of compound 6g (100 MHz, DMSO-d$_6$)
Figure S19. HRMS spectrum of compound 6g

* ¹H, ¹³C-NMR and HRMS of Compound 9a

Figure S20. ¹H NMR spectrum of compound 9a (400 MHz, DMSO-$_d$6)
Figure S21. $^{13}$C NMR spectrum of compound 9a (100 MHz, DMSO-$d_6$)

Figure S22. HRMS spectrum of compound 9a
- $^1$H, $^{13}$C-NMR and HRMS of Compound 9b

Figure S23. $^{13}$C NMR spectrum of compound 9b (100 MHz, DMSO-$d_6$)

Figure S24. $^1$H NMR spectrum of compound 9b (400 MHz, DMSO-$d_6$)
Figure S25. HRMS spectrum of compound 9b

- $^1$H, $^{13}$C-NMR and HRMS of Compound 9c

Figure S26. $^1$H NMR spectrum of compound 9c (400 MHz, DMSO-$d_6$)
Figure S27. $^{13}$C NMR spectrum of compound 9c (100 MHz, DMSO-$d_6$)

Figure S28. HRMS spectrum of compound 9c
- $^1$H, $^{13}$C-NMR and HRMS of Compound 9d

Figure S29. $^1$H NMR spectrum of compound 9d (400 MHz, DMSO-$d_6$)

Figure S30. $^{13}$C NMR spectrum of compound 9d (100 MHz, DMSO-$d_6$)
Figure S31. HRMS spectrum of compound 9d

- $^1$H, $^{13}$C-NMR and HRMS of Compound 9e

Figure S32. $^{13}$C NMR spectrum of compound 9e (100 MHz, DMSO-$d_6$)
Figure S33. $^1$H NMR spectrum of compound 9e (400 MHz, DMSO-$d_6$)

Figure S34. HRMS spectrum of compound 9e

- $^1$H, $^{13}$C-NMR and HRMS of Compound 9f
Figure S35. $^1$H NMR spectrum of compound 9f (400 MHz, DMSO-d$_6$)

Figure S36. $^{13}$C NMR spectrum of compound 9f (100 MHz, DMSO-d$_6$)
Figure S37. HRMS spectrum of compound 9f

- $^1$H, $^{13}$C-NMR and HRMS of Compound 9g

Figure S38. $^{13}$C NMR spectrum of compound 9g (100 MHz, DMSO-$d_6$)
Figure S39. $^1$H NMR spectrum of compound 9g (400 MHz, DMSO-$d_6$)

Figure S40. HRMS spectrum of compound 9g
- $^1$H, $^{13}$C-NMR and HRMS of Compound $9h$

Figure S41. $^1$H NMR spectrum of compound $9h$ (400 MHz, DMSO-$d_6$)

Figure S42. $^{13}$C NMR spectrum of compound $9h$ (100 MHz, DMSO-$d_6$)
Figure S43. HRMS spectrum of compound 9h

- $^1$H, $^{13}$C-NMR and HRMS of Compound 9i

Figure S44. $^1$H NMR spectrum of compound 9i (400 MHz, DMSO-$d_6$)
Figure S45. $^{13}$C NMR spectrum of compound 9i (100 MHz, DMSO-$d_6$)

Figure S46. HRMS spectrum of compound 9i
- $^1\text{H}, ^{13}\text{C}$-NMR and HRMS of Compound 10a

Figure S47. $^1$H NMR spectrum of compound 10a (400 MHz, DMSO-d$_6$)

Figure S48. $^{13}$C NMR spectrum of compound 10a (100 MHz, DMSO-d$_6$)
Figure S49. HRMS spectrum of compound 10a

- $^1$H, $^{13}$C-NMR and HRMS of Compound 10b

Figure S50. $^1$H NMR spectrum of compound 10b (400 MHz, DMSO-$d_6$)
Figure S51. $^{13}$C NMR spectrum of compound 10b (100 MHz, DMSO-$d_6$)

Figure S52. HRMS spectrum of compound 10b
- $^1$H, $^{13}$C-NMR and HRMS of Compound 10c

Figure S53. $^1$H NMR spectrum of compound 10c (400 MHz, DMSO-$d_6$)

Figure S54. $^{13}$C NMR spectrum of compound 10c (100 MHz, DMSO-$d_6$)
Figure S55. HRMS spectrum of compound 10c

- $^1$H, $^{13}$C-NMR and HRMS of Compound 10d

Figure S56. $^1$H NMR spectrum of compound 10d (400 MHz, DMSO-$d_6$)
Figure S57. $^{13}$C NMR spectrum of compound 10d (100 MHz, DMSO-$d_6$)

Figure S58. HRMS spectrum of compound 10d
- $^{1}H$, $^{13}C$-NMR and HRMS of Compound $^{10}e$

Figure S59. $^{1}H$ NMR spectrum of compound $^{10}e$ (400 MHz, DMSO-$d_{6}$)

Figure S60. $^{13}C$ NMR spectrum of compound $^{10}e$ (100 MHz, DMSO-$d_{6}$)
- $^1$H, $^{13}$C-NMR and HRMS of Compound 10f

Figure S61. HRMS spectrum of compound 10e

Figure S62. $^1$H NMR spectrum of compound 10f (400 MHz, DMSO-$d_6$)
Figure S63. $^{13}$C NMR spectrum of compound 10f (100 MHz, DMSO-$d_6$)

Figure S64. HRMS spectrum of compound 10f
- $^1$H, $^{13}$C-NMR and HRMS of Compound 11g

Figure S65. $^1$H NMR spectrum of compound 11g (400 MHz, DMSO-$d_6$)

Figure S66. $^{13}$C NMR spectrum of compound 10g (100 MHz, DMSO-$d_6$)
- **$^1$H, $^{13}$C-NMR and HRMS of Compound 10h**

Figure S67. HRMS spectrum of compound 10g

Figure S68. $^1$H NMR spectrum of compound 10h (400 MHz, DMSO-$d_6$)
Figure S69. $^{13}$C NMR spectrum of compound 10h (100 MHz, DMSO-$d_6$)

Figure S70. HRMS spectrum of compound 10h
- $^1$H, $^{13}$C-NMR and HRMS of Compound 10i
Figure S73. HRMS spectrum of compound 10i

- $^1$H, $^{13}$C-NMR and HRMS of Compound 10j

Figure S74. $^1$H NMR spectrum of compound 10j (400 MHz, DMSO-$d_6$)
Figure S75. $^{13}$C NMR spectrum of compound 10j (100 MHz, DMSO-$d_6$)

Figure S76. HRMS spectrum of compound 10j
- $^1$H, $^{13}$C-NMR and HRMS of Compound 11a

Figure S77. $^1$H NMR spectrum of compound 11a (400 MHz, DMSO-$d_6$)

Figure S78. $^{13}$C NMR spectrum of compound 11a (100 MHz, DMSO-$d_6$)
- $^1$H, $^{13}$C-NMR and HRMS of Compound 11b

Figure S79. $^1$H NMR spectrum of compound 11b (400 MHz, DMSO-$d_6$)

Figure S80. $^{13}$C NMR spectrum of compound 11b (100 MHz, DMSO-$d_6$)
Figure S81. HRMS spectrum of compound **11b**

- \(^1\)H, \(^{13}\)C-NMR and HRMS of Compound **11c**

Figure S82. \(^1\)H NMR spectrum of compound **11c** (400 MHz, DMSO-\textit{d}6)
Figure S83. $^{13}$C NMR spectrum of compound 11c (100 MHz, DMSO-$d_6$)

Figure S83. HRMS spectrum of compound 11c
- $^1$H, $^{13}$C-NMR and HRMS of Compound 11d

**Figure S84.** $^1$H NMR spectrum of compound 11d (400 MHz, DMSO-$d_6$)

**Figure S85.** $^{13}$C NMR spectrum of compound 11d (100 MHz, DMSO-$d_6$)
- $^{1}$H, $^{13}$C-NMR and HRMS of Compound 11e

Figure S86. HRMS spectrum of compound 11d

Figure S87. $^{1}$H NMR spectrum of compound 11e (400 MHz, DMSO-d$_6$)
Figure S88. $^{13}$C NMR spectrum of compound 11e (100 MHz, DMSO-$d_6$)

Figure S89. HRMS spectrum of compound 11e
• $^1$H, $^{13}$C-NMR and HRMS of Compound 11f

Figure S90. $^1$H NMR spectrum of compound 11f (400 MHz, DMSO-$d_6$)

Figure S91. $^{13}$C NMR spectrum of compound 11f (100 MHz, DMSO-$d_6$)
Figure S92. HRMS spectrum of compound 11f

- $^1$H, $^{13}$C-NMR and HRMS of Compound 11g

Figure S93. $^1$H NMR spectrum of compound 11g (400 MHz, DMSO-$d_6$)
Figure S94. $^{13}$C NMR spectrum of compound 11g (100 MHz, DMSO-$d_6$)

Figure S95. HRMS spectrum of compound 11g
- $^1$H, $^{13}$C-NMR and HRMS of Compound 11h

Figure S96. $^1$H NMR spectrum of compound 11h (400 MHz, DMSO-$d_6$)

Figure S97. $^{13}$C NMR spectrum of compound 11h (100 MHz, DMSO-$d_6$)
Figure S98. HRMS spectrum of compound 11h

- $^1$H, $^{13}$C-NMR and HRMS of Compound 11i

Figure S99. $^1$H NMR spectrum of compound 11i (400 MHz, DMSO-$d_6$)
Figure S100. $^{13}$C NMR spectrum of compound 11i (100 MHz, DMSO-$d_6$)

Figure S101. HRMS spectrum of compound 11i
- $^{1}H$, $^{13}C$-NMR and HRMS of Compound 11j

Figure S102. $^{1}H$ NMR spectrum of compound 11j (400 MHz, DMSO-$d_6$)

Figure S103. $^{13}C$ NMR spectrum of compound 11j (100 MHz, DMSO-$d_6$)
Figure S104. HRMS spectrum of compound 11j

- $^1$H, $^{13}$C-NMR and HRMS of Compound 14a

Figure S105. $^1$H NMR spectrum of compound 14a (400 MHz, DMSO-$d_6$)
Figure S106. $^{13}$C NMR spectrum of compound 14a (100 MHz, DMSO-$d_6$)

Figure S107. HRMS spectrum of compound 14a
- $^1$H, $^{13}$C-NMR and HRMS of Compound 14b

Figure S108. $^1$H NMR spectrum of compound 14b (400 MHz, DMSO-$d_6$)

Figure S109. $^{13}$C NMR spectrum of compound 14b (100 MHz, DMSO-$d_6$)
Figure S110. HRMS spectrum of compound 14b

- $^1$H, $^{13}$C-NMR and HRMS of Compound 14c

Figure S111. $^1$H NMR spectrum of compound 14c (400 MHz, DMSO-$d_6$)
Figure S112. $^{13}$C NMR spectrum of compound 14c (100 MHz, DMSO-$d_6$)

Figure S113. HRMS spectrum of compound 14c
● $^1$H, $^{13}$C-NMR and HRMS of Compound 14d

Figure S114. $^1$H NMR spectrum of compound 14d (400 MHz, DMSO-$d_6$)

Figure S115. $^{13}$C NMR spectrum of compound 14d (100 MHz, DMSO-$d_6$)
Figure S116. HRMS spectrum of compound 14d