

Design and Synthesis of 1,3,4-Thiadiazole Derivatives as Type IV Collagenase Inhibitors

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SUMMARY. Type IV collagenase is an essential metallopeptidase in the development of tumor invasion and angiogenesis. A series of novel low molecular-weight 1,3,4-thiadiazole derivatives were designed and synthesized as antitumor agents. The structures were confirmed by IR, ¹H-NMR, and MS. Some of the target compounds display excellent potency toward MMP-2 and MMP-9 with inhibition rate > 50% at 10 μM, meanwhile the selectivity towards MMP-9 is higher than towards MMP-2, and could be used as lead compounds for exploring new type IV collagenase inhibitors in the future.

RESUMEN. La colagenasa tipo IV es una metalopeptidasa esencial en el desarrollo de la invasión tumoral y la angiogénesis. Una serie de nuevos derivados de 1,3,4-tiadiazol de bajo peso molecular fueron diseñados y sintetizados como agentes antitumorales. Las estructuras se confirmaron por IR, ¹H-NMR y MS. Algunos de los compuestos diana mostraron excelente potencial sobre MMP-2 y MMP-9, con tasas de inhibición > 50% a una concentración de 10 μM; la selectividad hacia MMP-9 es mayor que hacia MMP-2, por lo que podrían ser utilizados como compuestos líderes para explorar nuevos inhibidores de la colagenasa tipo IV en el futuro.

KEY WORDS: enzyme inhibitors, MMP-2, MMP-9, synthesis, type IV collagenase.

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