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Cytotoxic Investigation of Isophthaloyl Cyclopentapeptides

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SUMMARY. The anticancer activities for nine newly designed and synthesized Cyclo-[N$^{\alpha}$-Isophthaloyl-*bis*-(Glycine-Amino Acid)-L-Lysine]-X cyclopeptide candidates were investigated. Eight cancer cell lines, representing different types of human cancers, were targeted by such candidates. Comparative cytotoxicity data with those of five common anticancer standard drugs were identically realized. In particular, the cylcopentapeptides Cyclo-[N$^{\alpha}$-isophthaloyl-*bis*-(Gly-Sar)-L-Lys]-OMe, (**13**) and Cyclo-[N$^{\alpha}$-isophthaloyl-*bis*-(Gly-Sar)-L-Lys]-OH (**16**) showed a higher anticancer activity compared to commercially available anticancer drugs. The cylcopentapeptides: Cyclo-[N$^{\alpha}$-isophthaloyl-*bis*-(Gly-Gly)-L-Lys]-$NHNH_2$ (**17**) and Cyclo-[N$^{\alpha}$-isophthaloyl-*bis*-(Gly-Sar)-L-Lys]-$NHNH_2$ (**19**) were found more potent than some of the tested anticancer drugs. It would be concluded that the suggested molecular structural features for these novel isopthaloyl bridged cyclopeptides seemed significant for, prospectively, investigable novel anticancer candidates.

RESUMEN. Se investigaron las actividades anticancerosas de nueve candidatos sintetizados de ciclopéptido Ciclo-[N$^{\alpha}$-Isoftaloil-*bis*-(Glicina-Aminoácido)-L-Lisina]-X de nuevo diseño y ocho líneas celulares de cáncer, que representan diferentes tipos de cánceres humanos. Los datos comparativos de citotoxicidad con los de cinco fármacos comunes anticancerígenos estándar se realizaron de forma idéntica. En particular, los ciclopentapéptidos Ciclo-[N$^{\alpha}$-isoftaloil-*bis*-(Gly-Sar)-L-Lys]-OMe (**13**) y Ciclo-[N$^{\alpha}$-isoftaloil-*bis*-(Gly-Sar)-L-Lys]-OH (**16**) mostraron una mayor actividad anticancerígena en comparación con los fármacos anticancerígenos comercialmente disponibles. Los ciclopentapéptidos: Ciclo-[N$^{\alpha}$-isoftaloil-*bis*-(Gly-Gly)-L-Lys]-$NHNH_2$ (**17**) y Ciclo-[N$^{\alpha}$-isoftaloil-*bis*-(Gly-Sar)-L-Lys]-$NHNH_2$ (**19**) resultaron más potentes que algunos de los fármacos anticancerígenos probados. Se concluiría que las características estructurales moleculares sugeridas para estos nuevos ciclopéptidos puenteados con isoptaloilo parecían significativas para ser, prospectivamente, nuevos candidatos anticancerígenos investigables.

KEY WORDS: amino acids, anticancers, cytotoxicity, cyclopeptides, peptide synthesis.

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