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CENTRO DE INVESTIGACIÓN BIOMÉDICA EN RED Diabetes y Enfermedades Metabólicas Asociadas
IDiBE UNIVERSITAS Miguel Hernández

IMPACTO DE UNA MEZCLA DE DISRUPTORES ENDOCRINOS EN LA VIABILIDAD Y FUNCIÓN DE CÉLULAS β PANCREÁTICAS BAJO ESTRÉS VIRAL

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Introducción y Objetivos: La diabetes tipo 1 (DT1) es una enfermedad autoinmune caracterizada por la destrucción progresiva de las células β pancreáticas. El aumento de su incidencia en las últimas décadas sugiere un papel relevante de factores ambientales, entre ellos las infecciones virales y la exposición a disruptores endocrinos. El objetivo de este estudio fue evaluar el efecto de una mezcla de disruptores endocrinos (EDCs), a concentraciones ambientalmente relevantes, sobre la viabilidad y la función de las células β, así como su interacción con un mimético de infección viral.

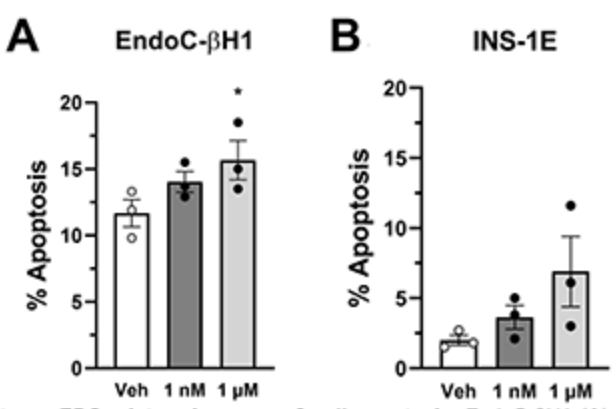

Fig. 1. Exposure to an EDC mixture increases β-cell apoptosis. EndoC-βH1 (**A**) and INS-1E (**B**) cells were treated for 24 h with Vehicle (white bars), 1 nM (dark gray bars) or 1 μM EDC mixture (light gray bars). Apoptosis was evaluated using HO and PI staining. Data represent mean ± SEM (n=3 independent experiments). *p≤0.05 vs vehicle. One-way ANOVA.

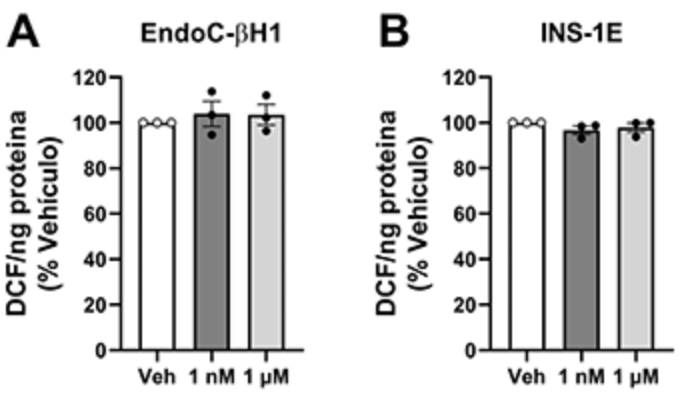

Fig. 2. Exposure to an EDC mixture does not change ROS production. EndoC-βH1 (**A**) and INS-1E (**B**) cells were treated for 24 h with Vehicle (white bars), 1 nM (dark gray bars) or 1 μM EDC mixture (light gray bars). ROS production was measured by the oxidation of the fluorescent probe DCF and normalised to total protein. Data represent mean ± SEM (n=3 independent experiments).

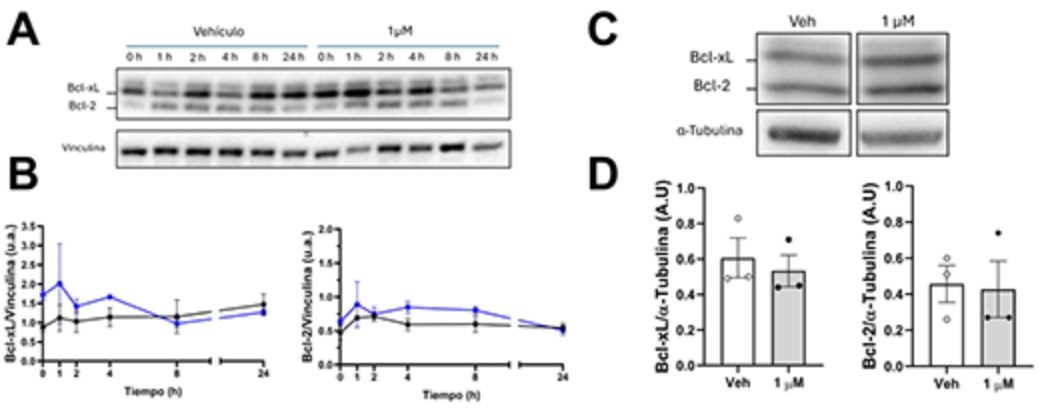

Fig. 3. Exposure to an EDC mixture does not change Bcl-2 and Bcl-xL expression. EndoC-βH1 (**A,B**) and INS-1E (**C,D**) cells were treated for 24 h with Vehicle (white bars) or 1 μM EDC mixture (blue line or light gray bars). Protein expression was measured by Western blot. (A,C) Representative images of three independent experiments. Data represent mean ± SEM (n=3 independent experiments).

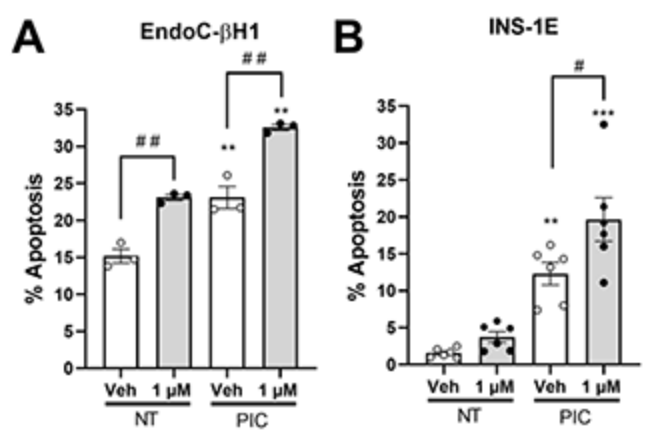

Fig. 4. Exposure to an EDC mixture increases β-cell apoptosis in poly(I:C)-treated cells. EndoC-βH1 (**A**) and INS-1E (**B**) cells were treated for 24 h with Vehicle (white bars) or 1 μM EDC mixture (gray bars), in the absence (NT) or presence of poly(I:C) (1 μg/ml). Apoptosis was evaluated using HO and PI staining. Data represent mean ± SEM (n=3-6 independent experiments). **p≤0.01, ***p≤0.001 vs NT control; #p≤0.05, ##p≤0.01 vs vehicle. Two-way ANOVA.

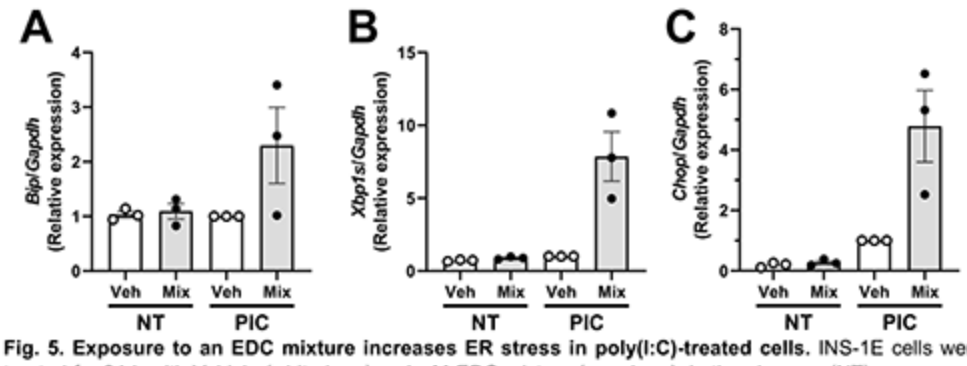

Fig. 5. Exposure to an EDC mixture increases ER stress in poly(I:C)-treated cells. INS-1E cells were treated for 24 h with Vehicle (white bars) or 1 μM EDC mixture (gray bars), in the absence (NT) or presence of poly(I:C) (1 μg/ml). mRNA expression of *Bip* (**A**), *Xbp1s* (**B**), and *Chop* (**C**) was measured by qRT-PCR, normalized to the housekeeping gene *Gapdh*, and then by Vehicle/PIC-treated cells (considered as 1). Data represent mean ± SEM (n=3 independent experiments).

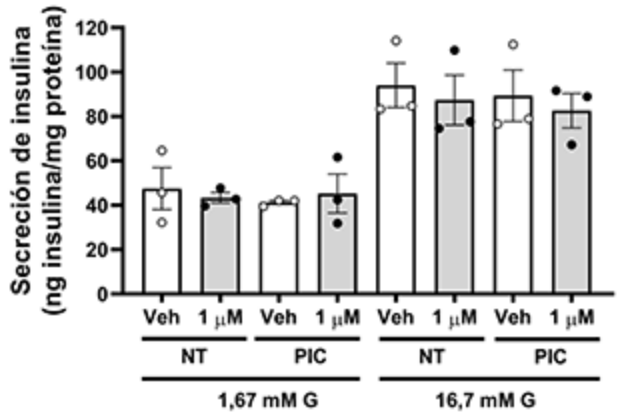

Fig. 6. Exposure to an EDC mixture does not change glucose-stimulated insulin secretion in poly(I:C)-treated cells. MIN6 cells were treated for 24 h with Vehicle (white bars) or 1 μM EDC mixture (gray bars), in the absence (NT) or presence of poly(I:C) (1 μg/ml). Insulin released into the medium was measured by ELISA. Data represent mean ± SEM (n=3 independent experiments).

Conclusión: La exposición a mezclas de disruptores endocrinos, incluso a concentraciones ambientalmente relevantes, compromete la supervivencia de las células β, especialmente en condiciones de estrés viral. Estos efectos se asocian a la activación de vías apoptóticas y de estrés del retículo endoplasmático, sin un impacto detectable sobre la función secretora a corto plazo. En conjunto, estos resultados apoyan la hipótesis de que la exposición crónica a disruptores endocrinos podría aumentar la vulnerabilidad de las células β y contribuir al desarrollo de DT1 en individuos genéticamente predispuestos.

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