

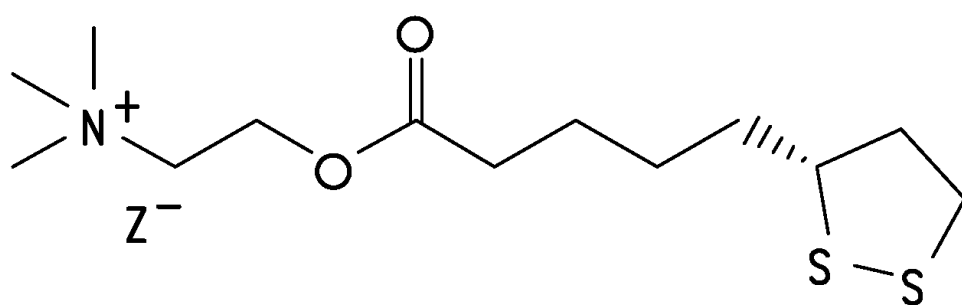


FIG.1

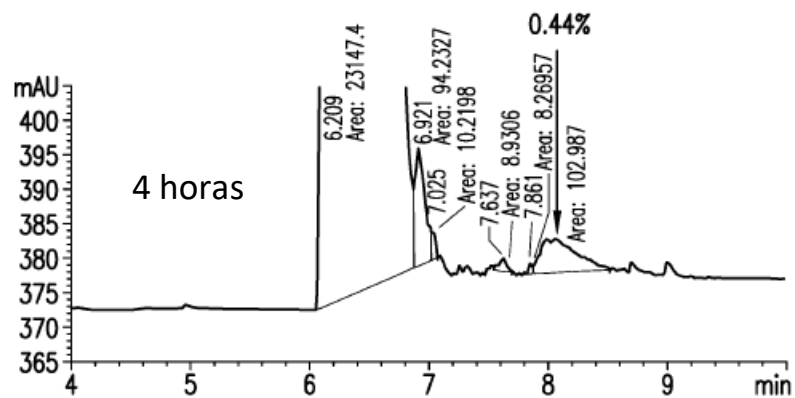
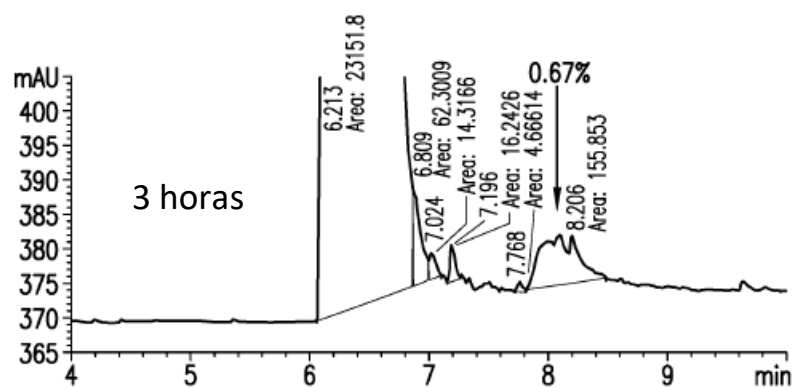
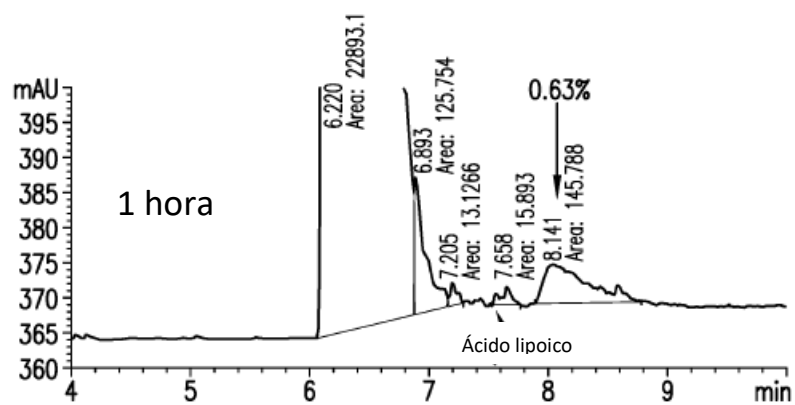


FIGURA 2

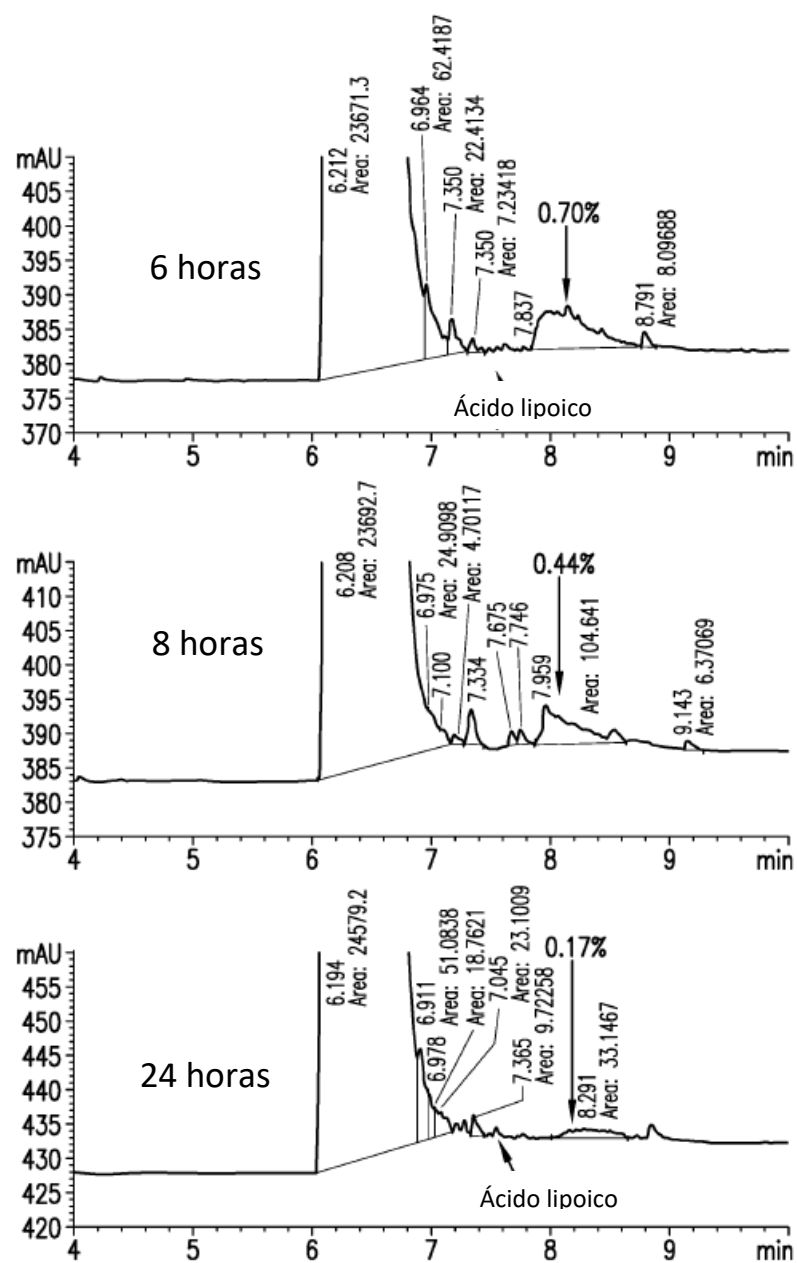


FIGURA 3

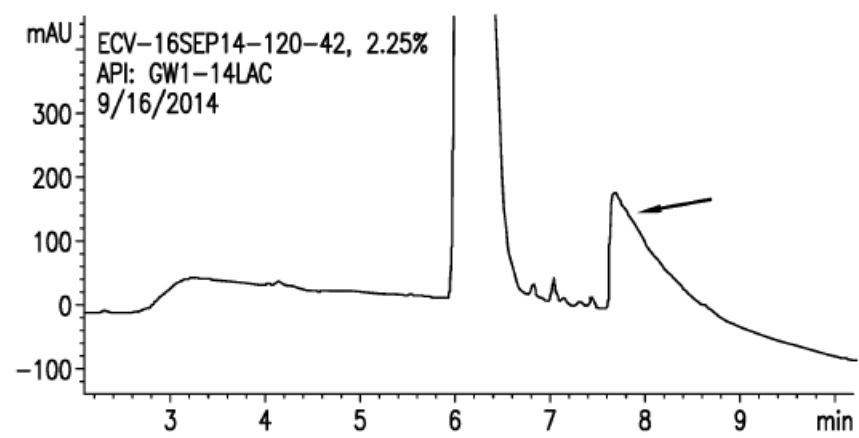


FIGURA 4

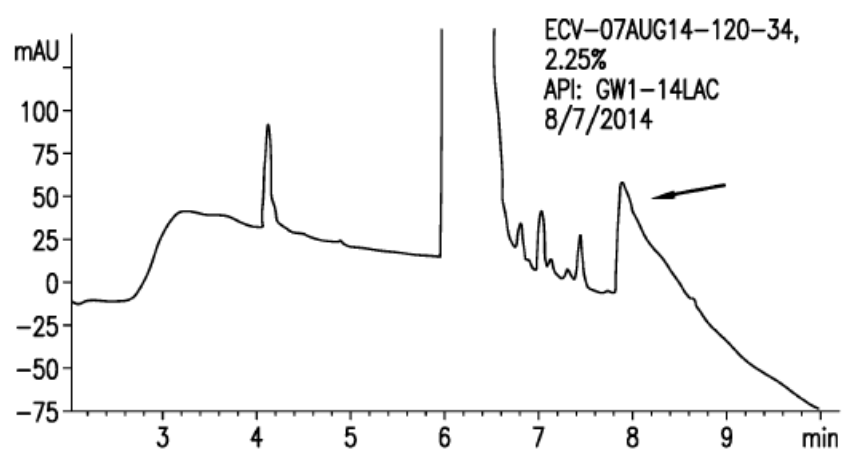


FIGURA 5A

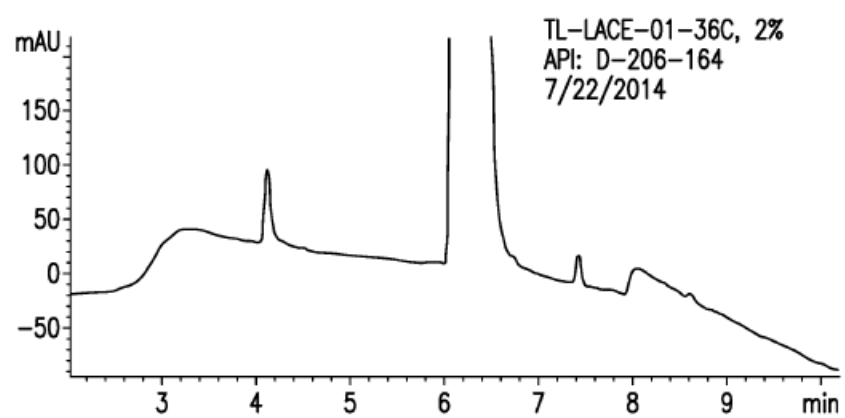
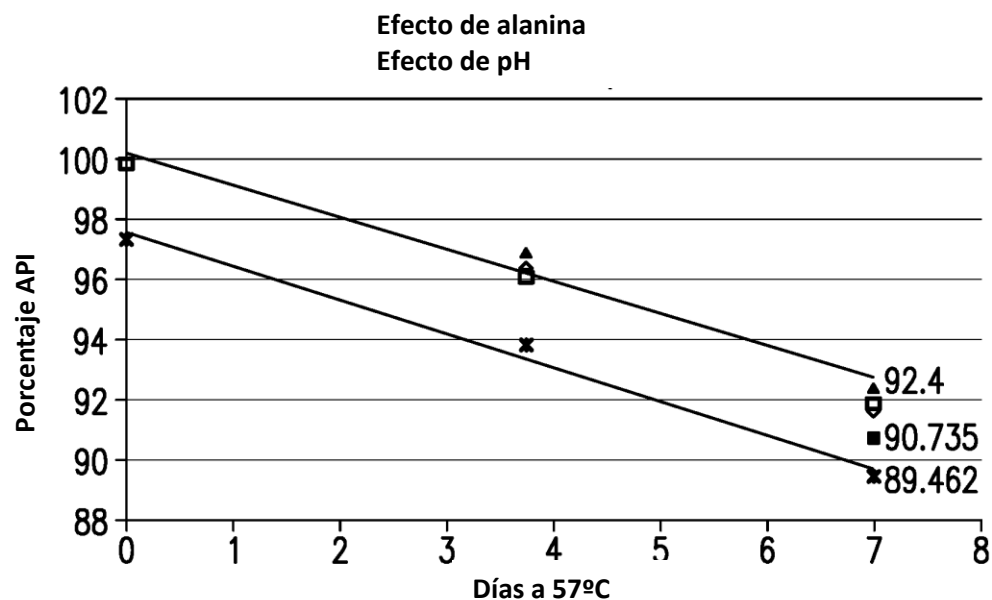


FIGURA 5B



- ◇ Control-Original
- Control @ pH 3.5
- ▲ Control @ pH 4
- Control @ pH 5
- * Control con Alanina

$$y = -1.0608x + 100.19$$

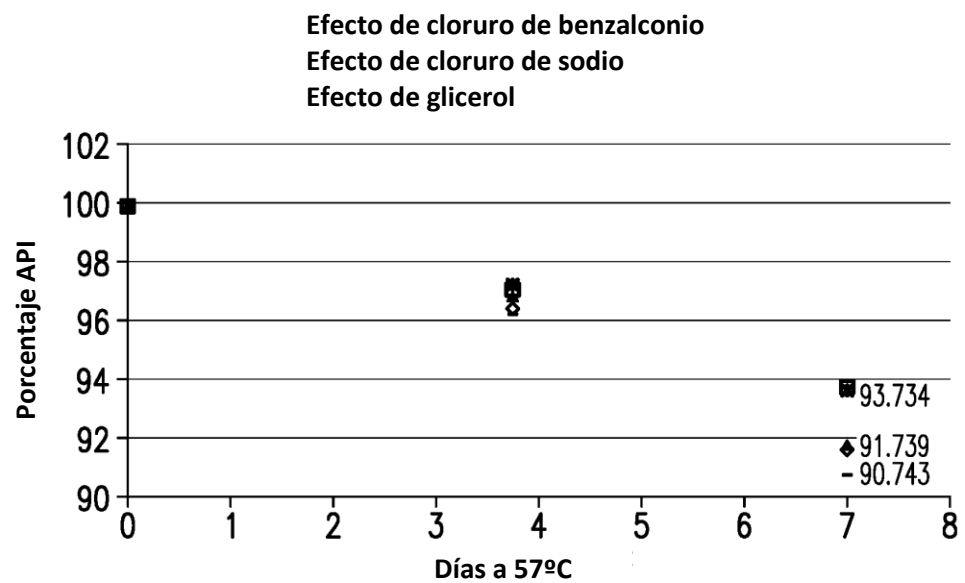
$$R^2 = 0.9757$$

Alanina tiene un efecto positivo
La formulación es estable entre pH 3.5-5

$$y = -1.1205x + 97.558$$

$$R^2 = 0.9893$$

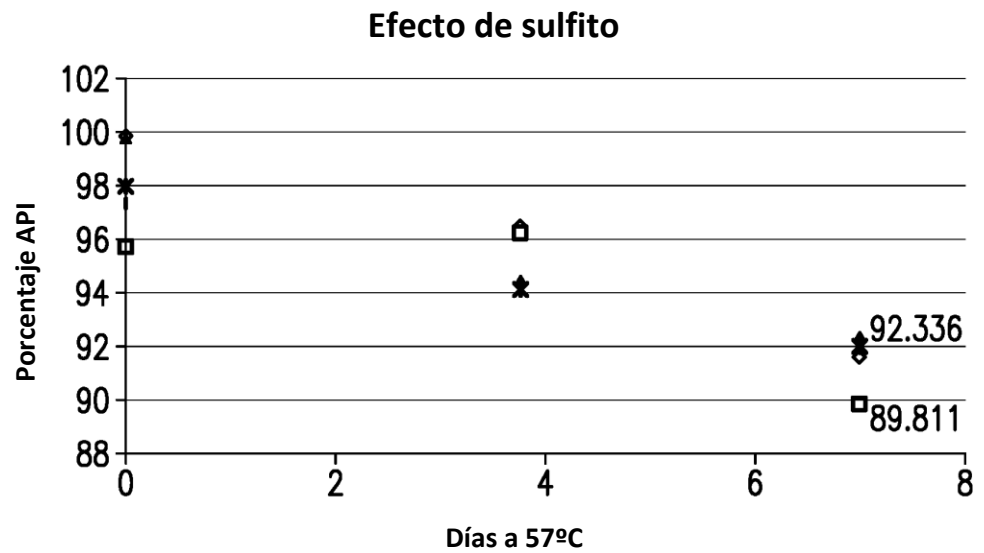
FIG.6



1. El cloruro de sodio tiene un efecto nocivo
2. La ausencia de cloruro de benzalconio puede tener un impacto positivo
3. La ausencia de glicerol puede tener un efecto positivo

- ◇ Control–Original
- Control con 0.25% NaCl
- ▲ Control menos glicerol, con 0.9% NaCl
- Control sin BAC, pH 4.5
- ✕ Control sin Glicerol, pH 4.5

FIG.7



◇ Control-Original

▲ Control + 0.05% Sulfite, pH 4

□ Control + 0.05% Sulfite, pH 4.5

✱ Control + 0.1% Sulfite, pH 4.5

1. El sulfito parece tener un efecto nocivo

FIG.8

Prototipos de formulación libres de cloruro de benzalconio

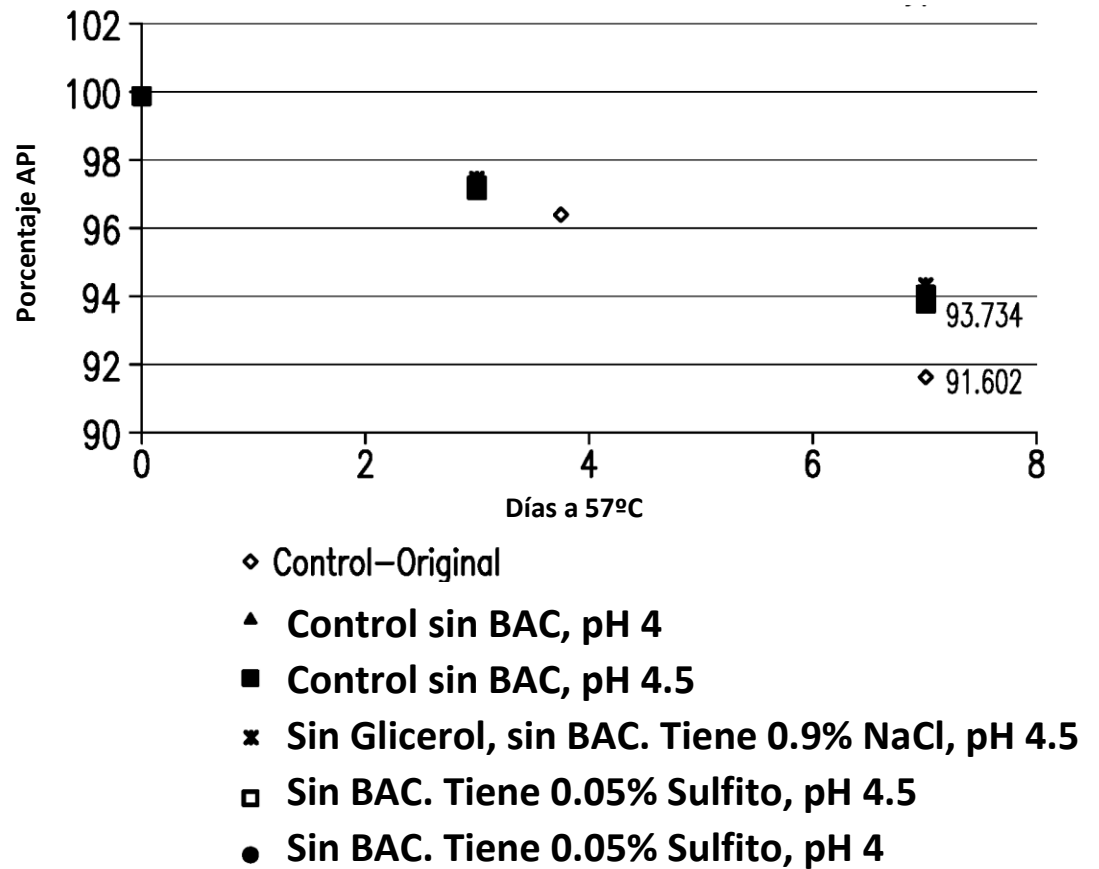
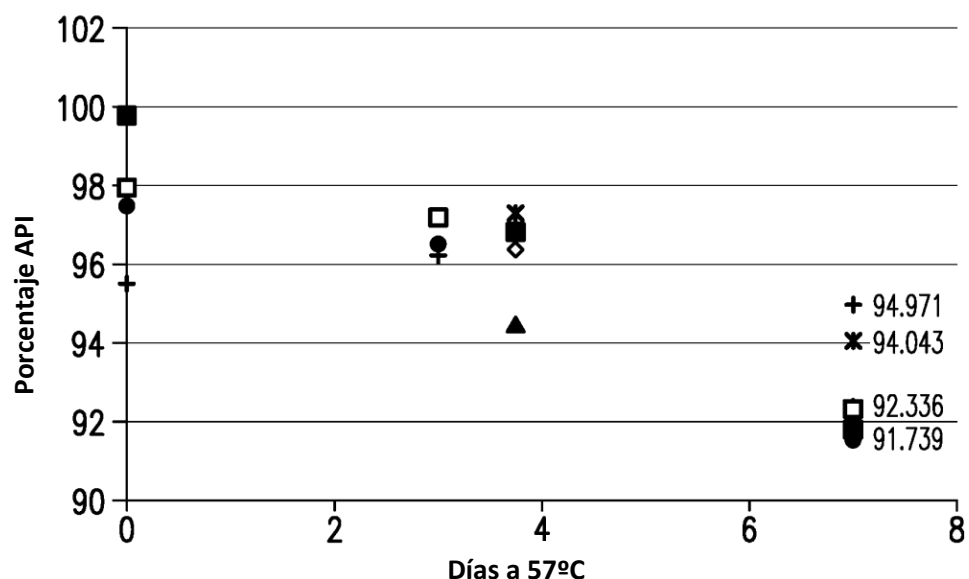


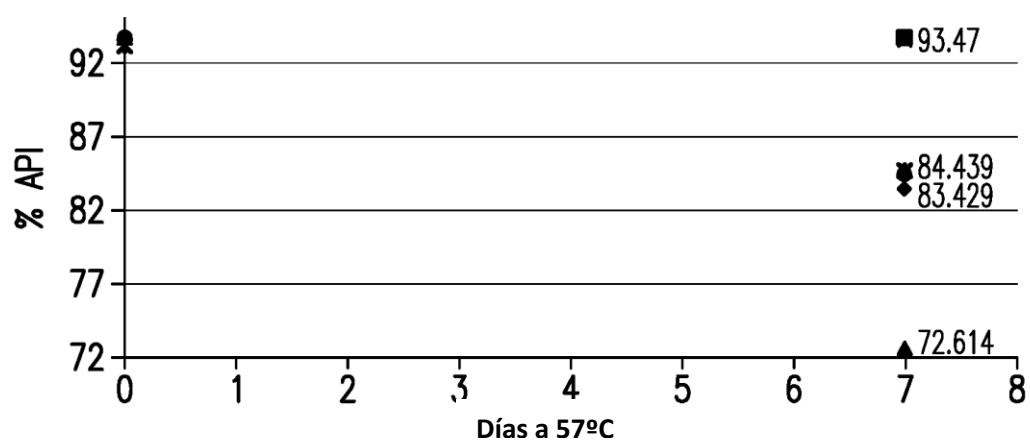
FIG.9

Efecto de cloruro de sodio + combinaciones de sulfito, sin glicerol



- ◇ Control-Original
- ▲ Control con 0.25% NaCl
- Control menos Glicerol, con 0.9% NaCl
- × Sin Glicerol. Tiene 0.9% NaCl y 0.05% Sulfito, pH 3.5
- Sin Glicerol. Tiene 0.9% NaCl y 0.05% Sulfito, pH 4
- Sin Glicerol. Tiene 0.9% NaCl y 0.05% Sulfito, pH 4.5
- + Sin Glicerol, sin BAC. Tiene 0.9% NaCl y 0.05% Sulfito, pH 4

FIG.10



- ◇ Control - Original
- pH 4.5 Tampón acetato
- ▲ pH 7.5 Tampón borato
- × pH 4.5 Tampón acetato + ácido bórico
- ⌘ pH 4.5 Tampón acetato + EDTA
- pH 4.5 Tampón acetato + ácido bórico y EDTA

FIG.1 1

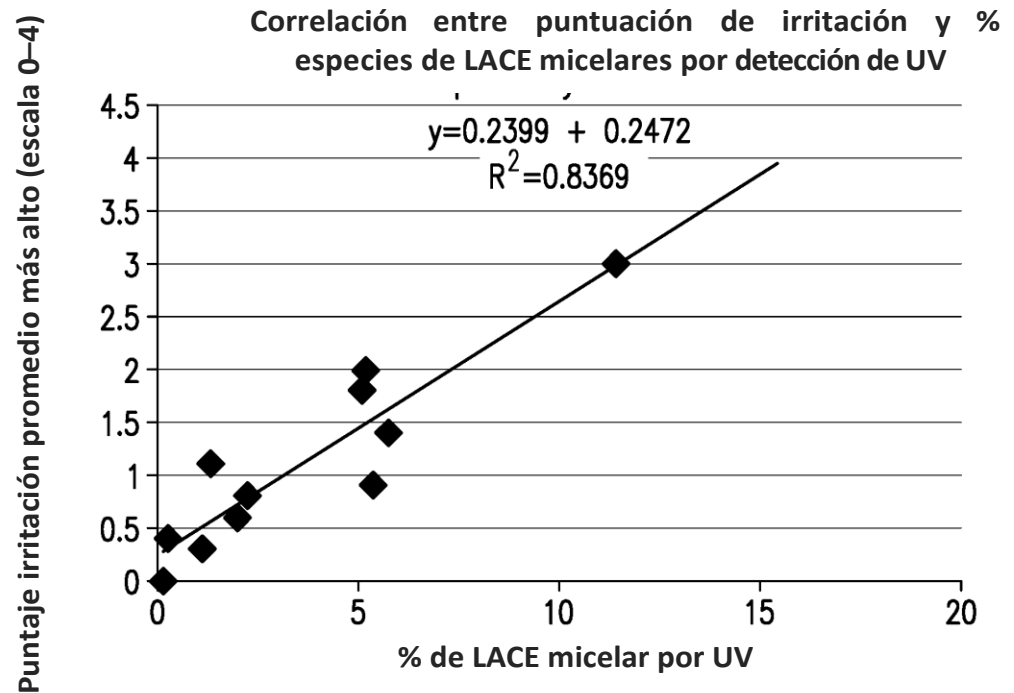


FIG.12A

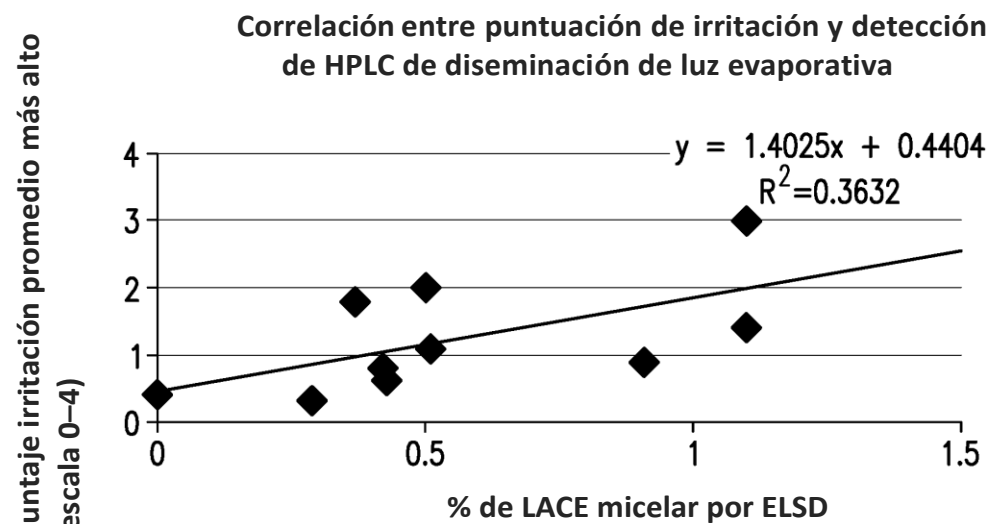


FIG.12B

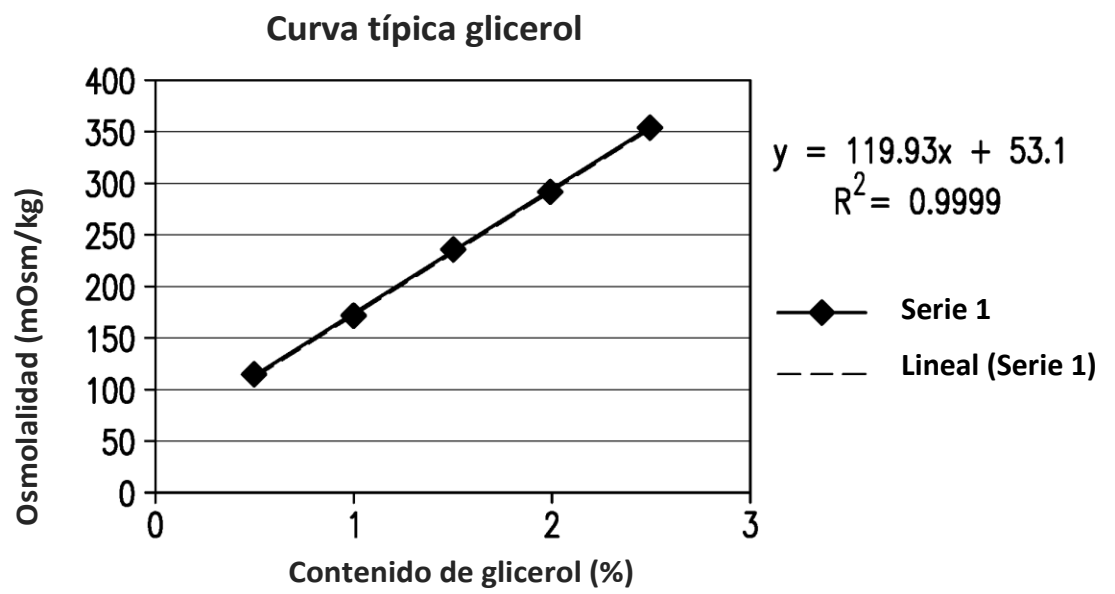


FIG.12C

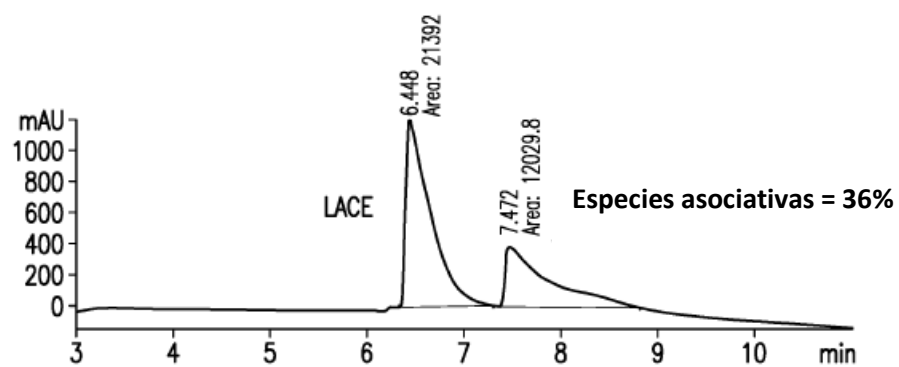


FIG.13A

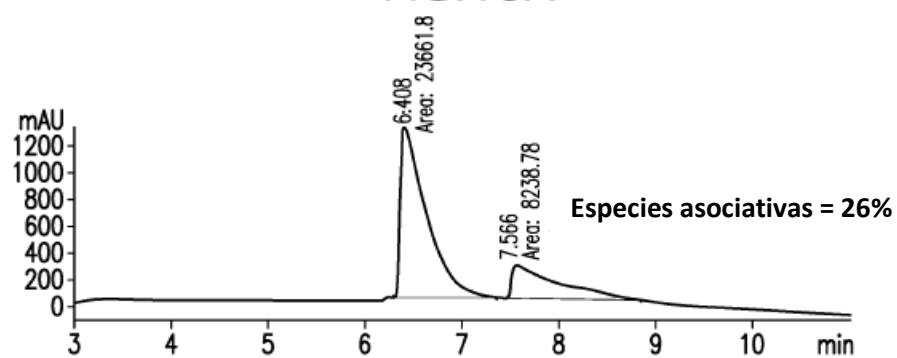


FIG.13B

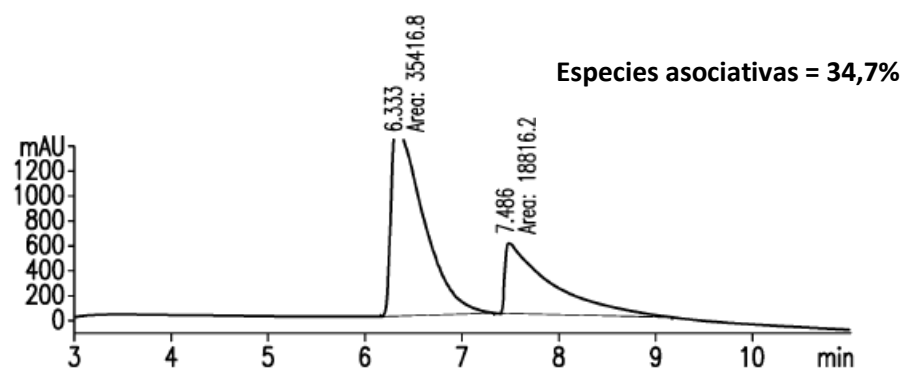


FIG.13C

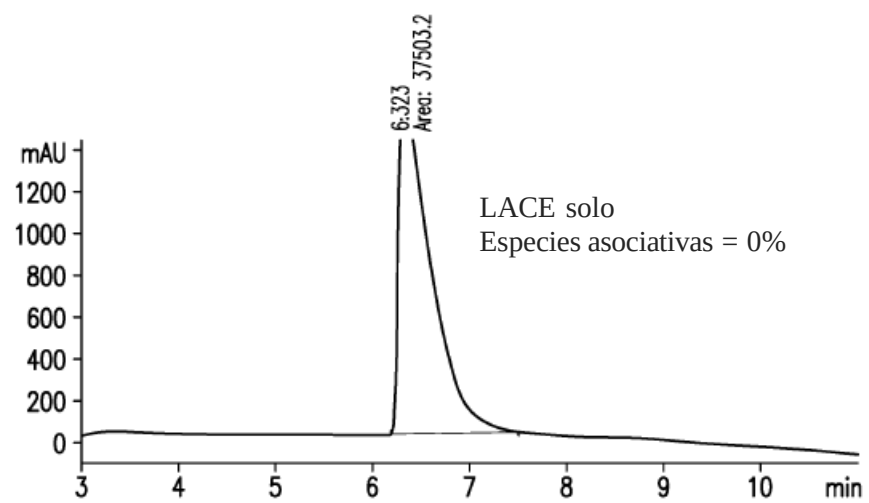


FIGURA 14

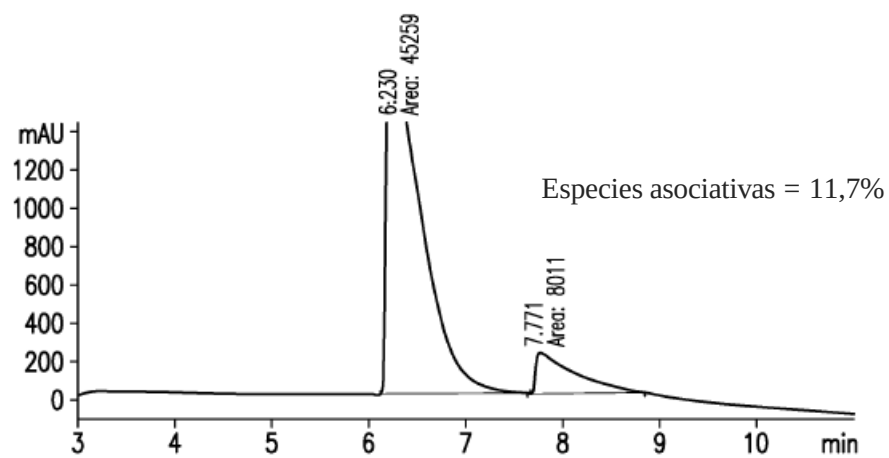


FIGURA 15

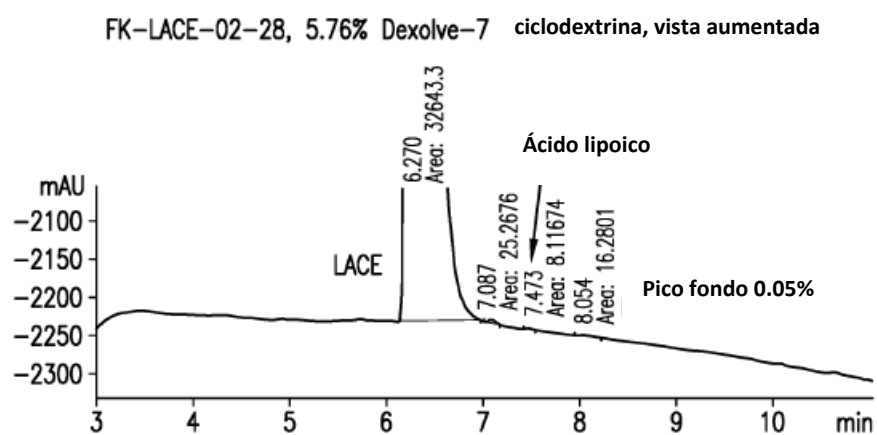
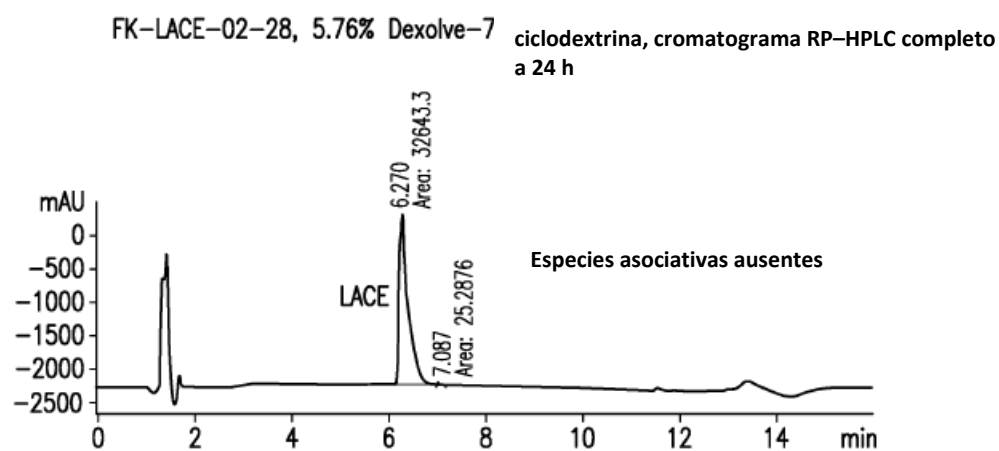
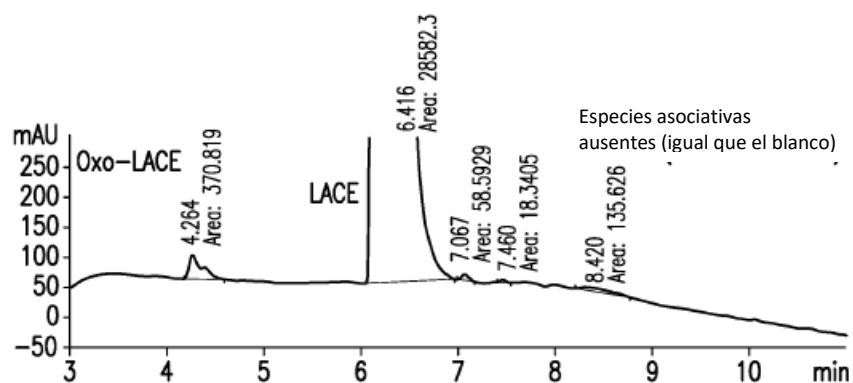


FIGURA 16

FK-LACE-02-29, 5% Polipropilenglicol, cromatograma RP-HPLC a 72 h



- LACE oxidado probablemente debido a 100 ppm peróxidos en material inicial PPG
- Los peróxidos son una impureza común de polímeros de poliéter tales como PEG y PPG, que se originan de la reacción con oxígeno. La formación de peróxidos puede evitarse mediante el almacenamiento bajo nitrógeno a temperaturas frías.

FIGURA 17

Efecto de HP- β -CD sobre estabilidad de LACE frente a la oxidación

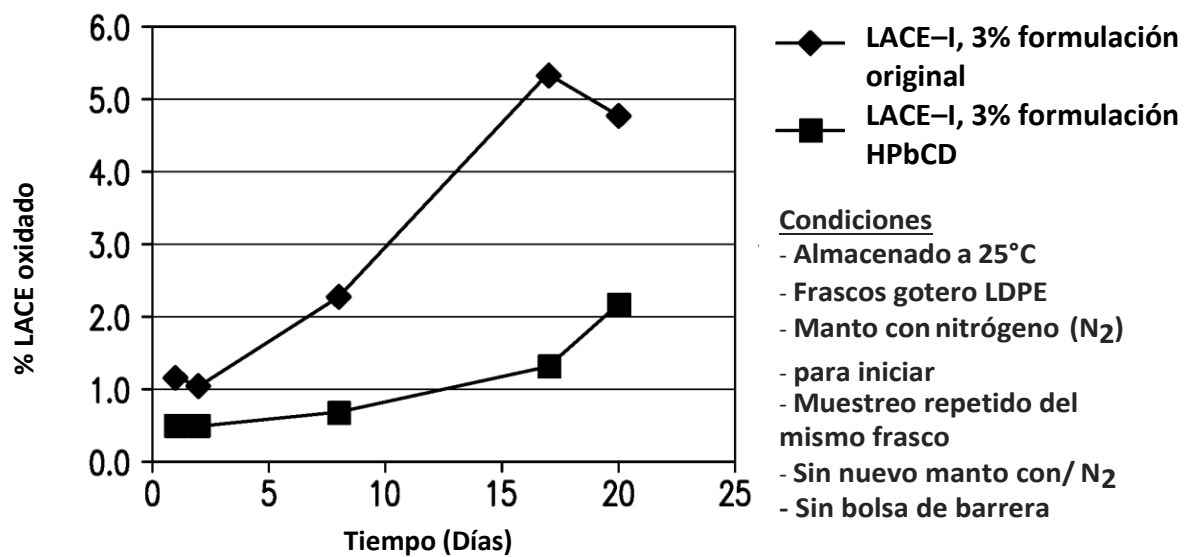


FIG.18

Efecto de HP- β -CD sobre estabilidad de LACE-yoduro

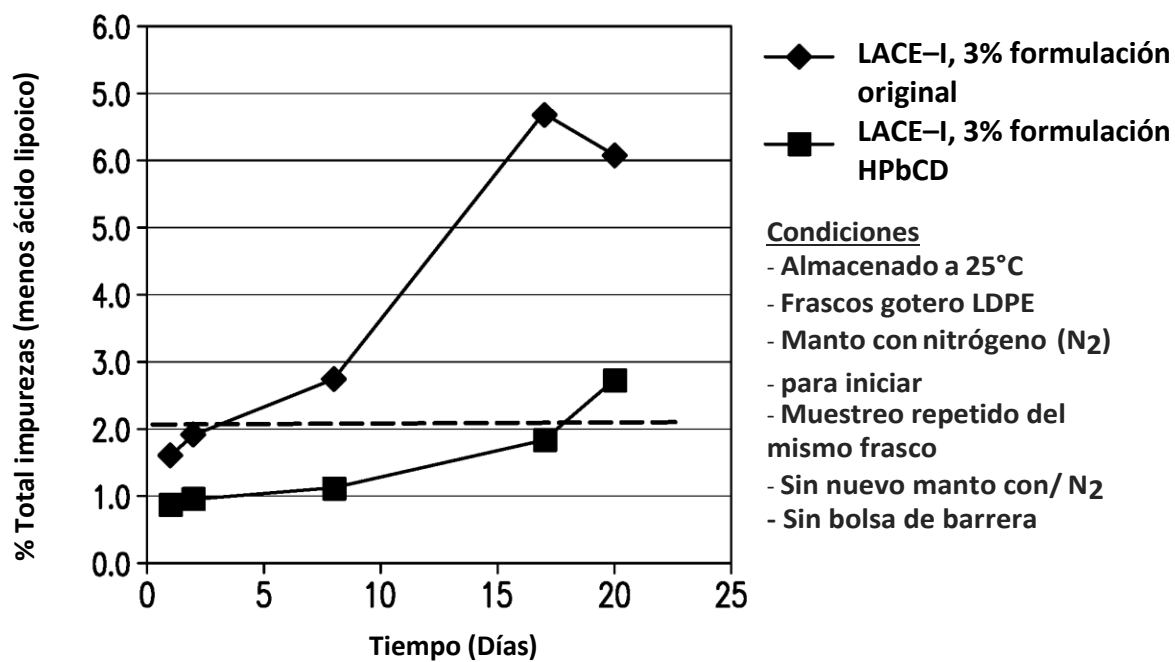


FIG.19

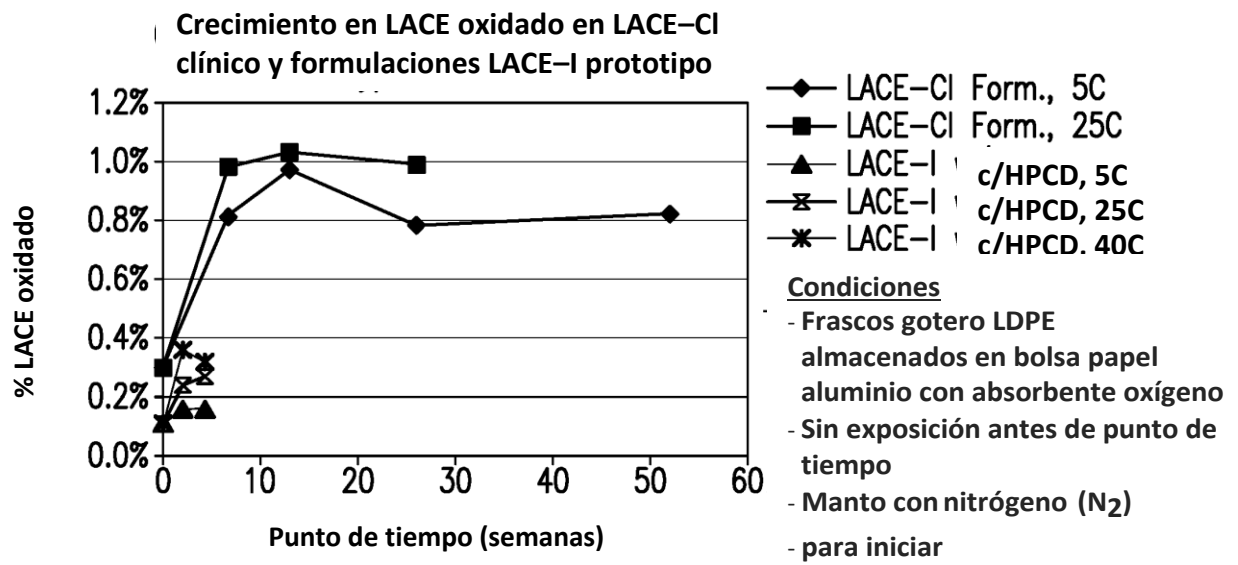


FIG.20

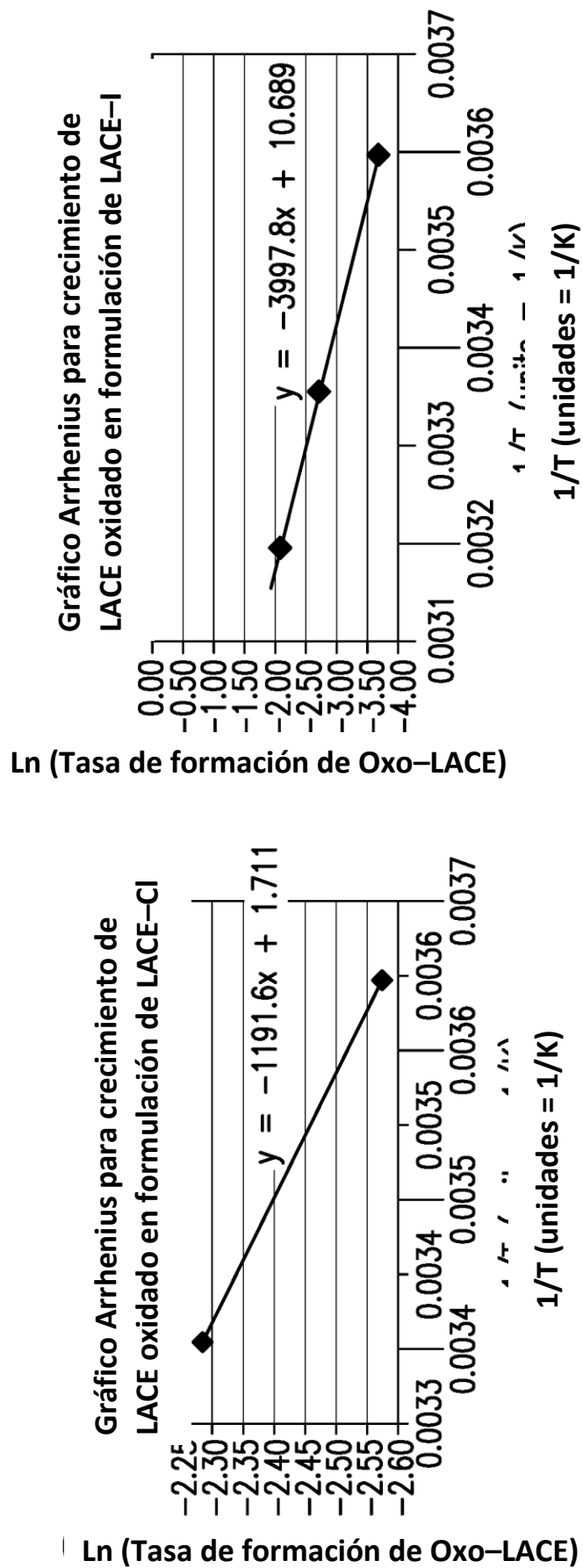


FIG.21

Gráfico Arrhenius para crecimiento de ácido lipoico en formulación de LACE–Cl

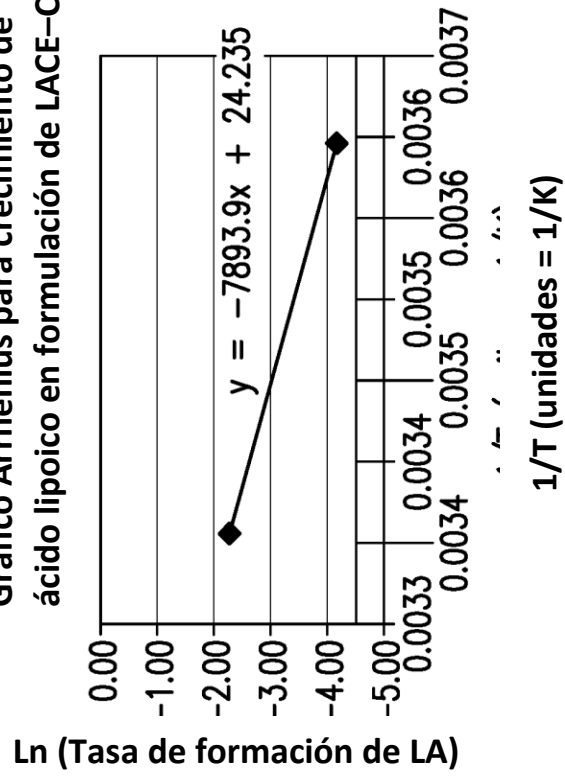


Gráfico Arrhenius para crecimiento de ácido lipoico en formulación de LACE–I

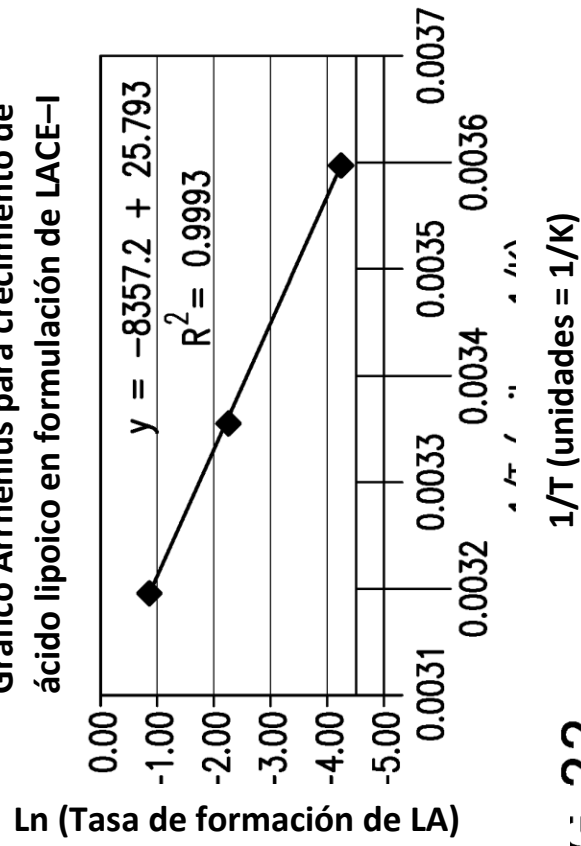


FIG. 22

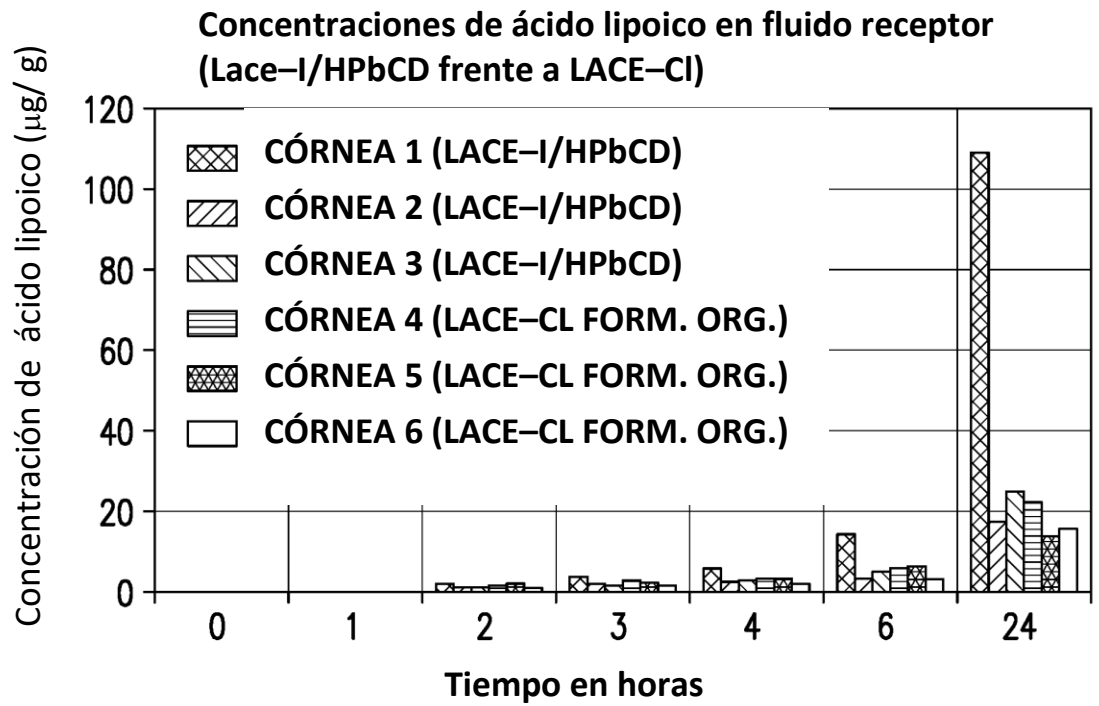


FIG.24

**Concentraciones de LACE en fluido receptor
(Lace-I/HPbCD frente a LACE-Cl)**

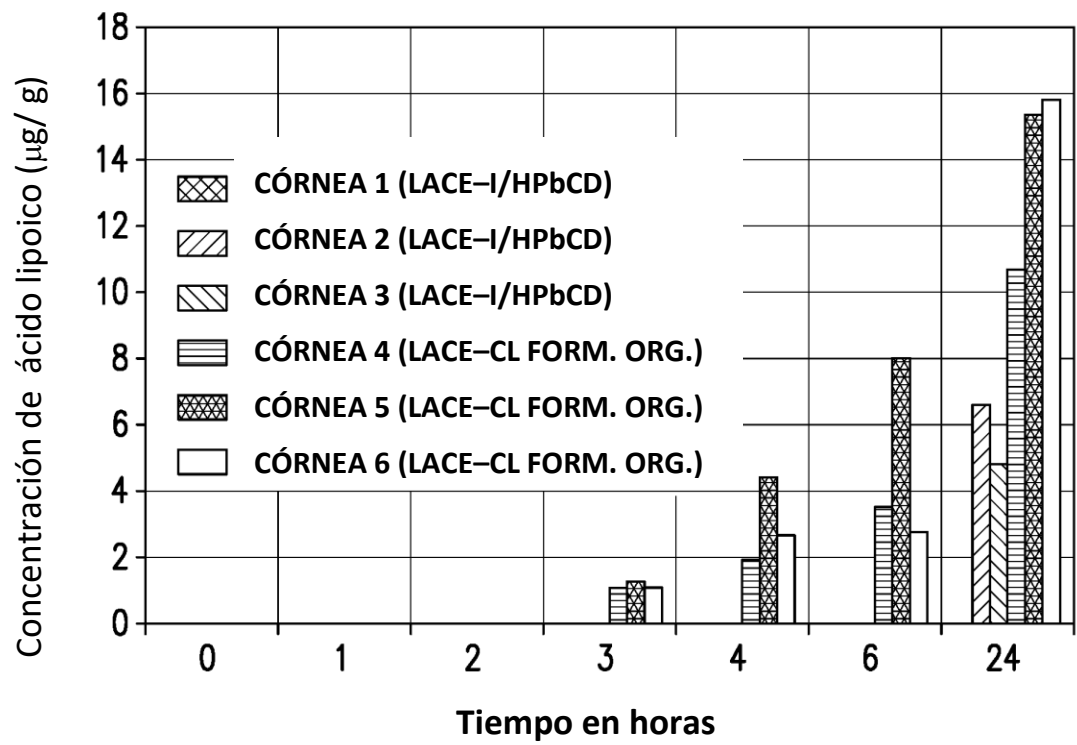


FIG.25

**Concentraciones de ácido lipoico en fluido receptor
(3% LACE-I/HPbCD frente a 4.5% LACE-I/HPbCD), Córneas 2–6**

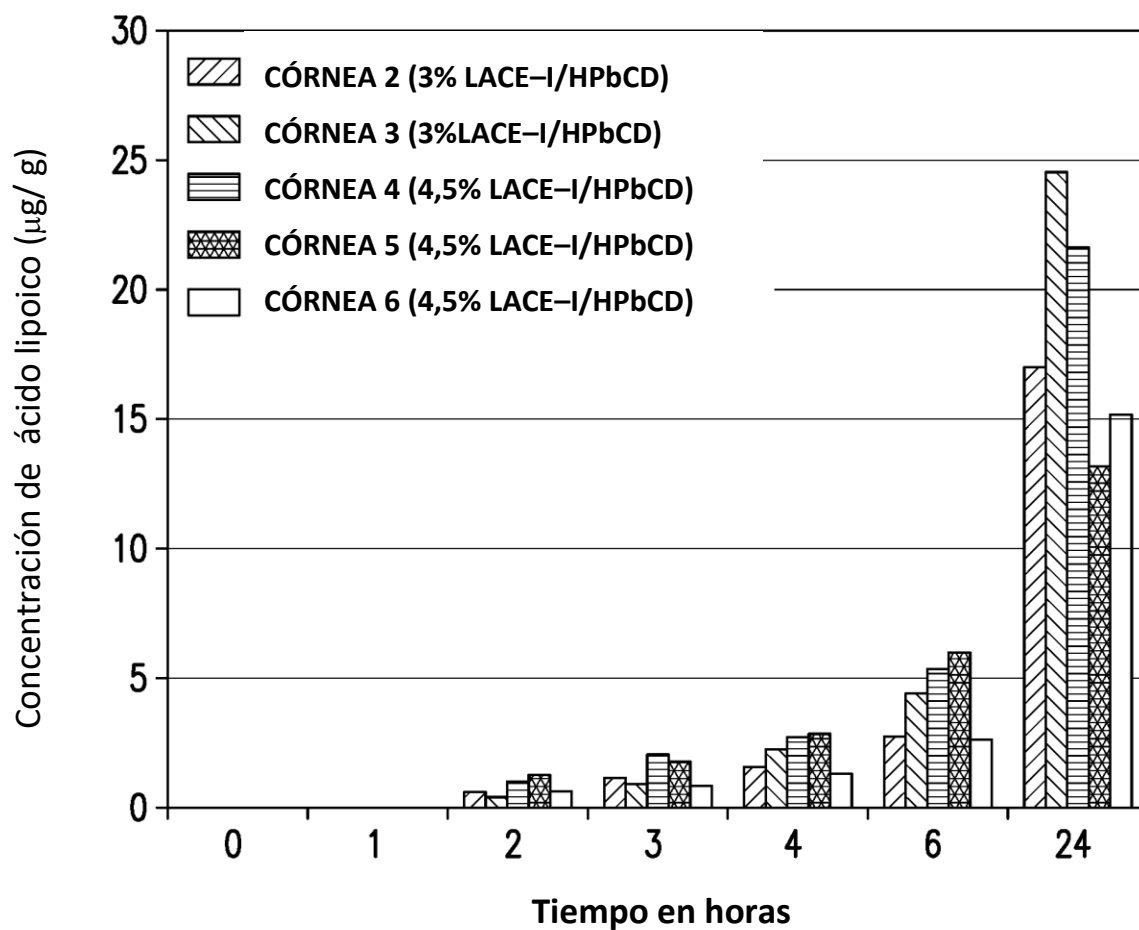


FIG.26

Extracción de ácido lipoico de sección corneal

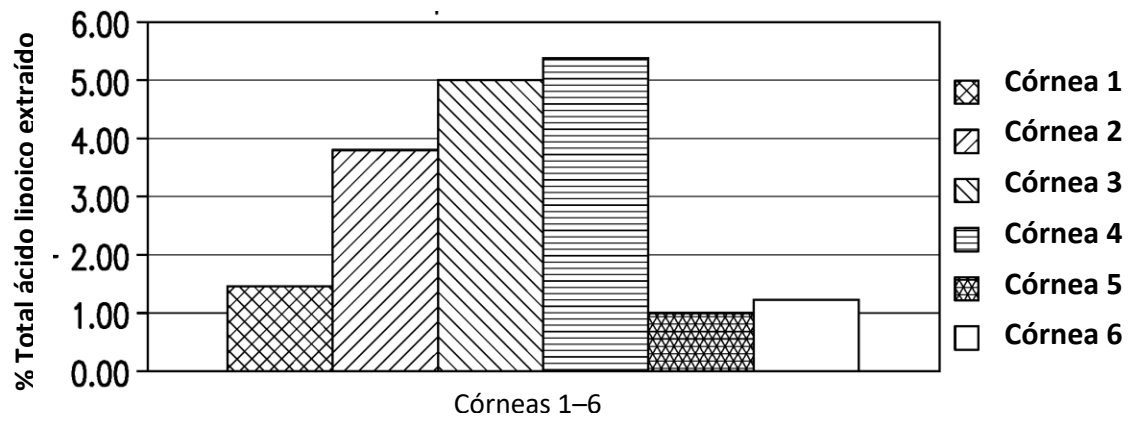


FIG.27

**Concentración de ácido lipoico en fluido receptor
(4,5% LACE-I/HPbCD frente a 1,5% LACE-Cl)**

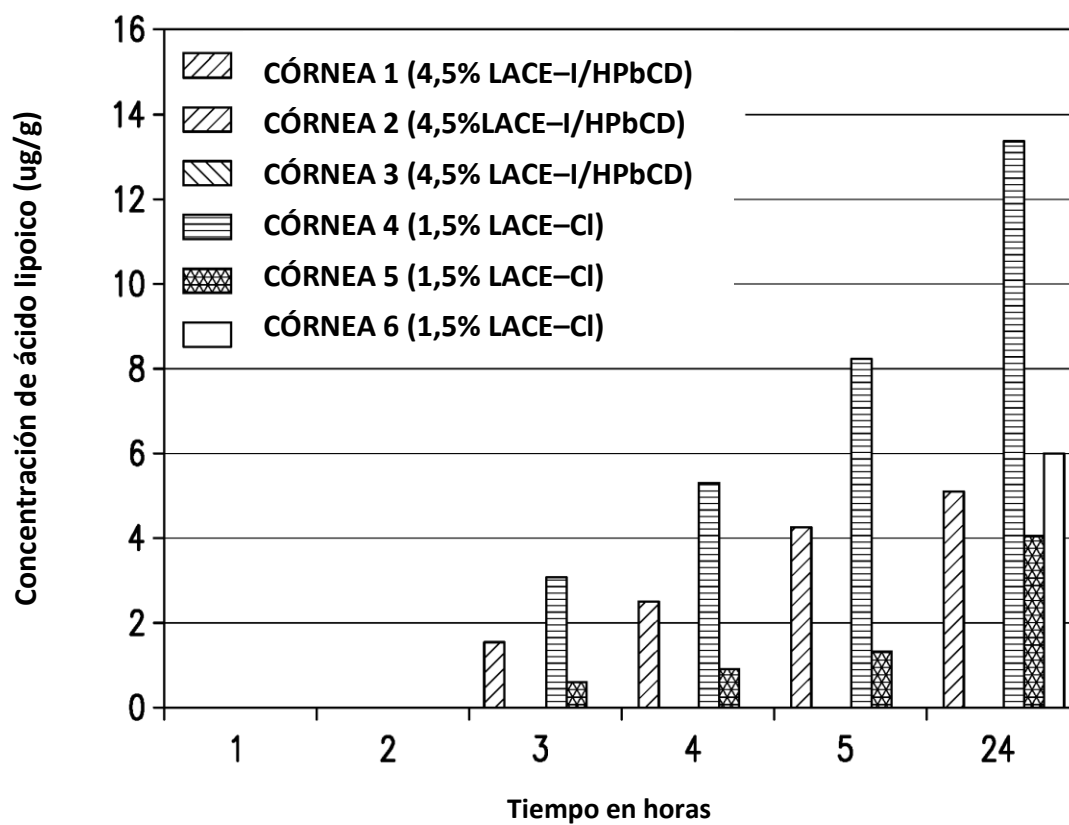


FIG.28

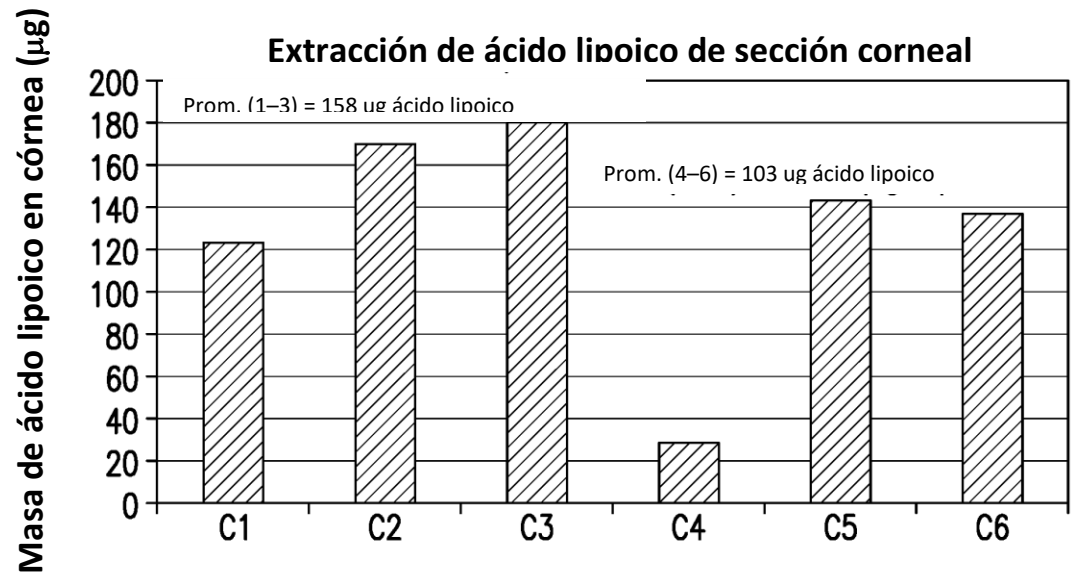


FIG.29

**Concentraciones de ácido lipoico en fluido receptor
(7,4% LACE-I/HPbCD frente a 0% HPbCD)**

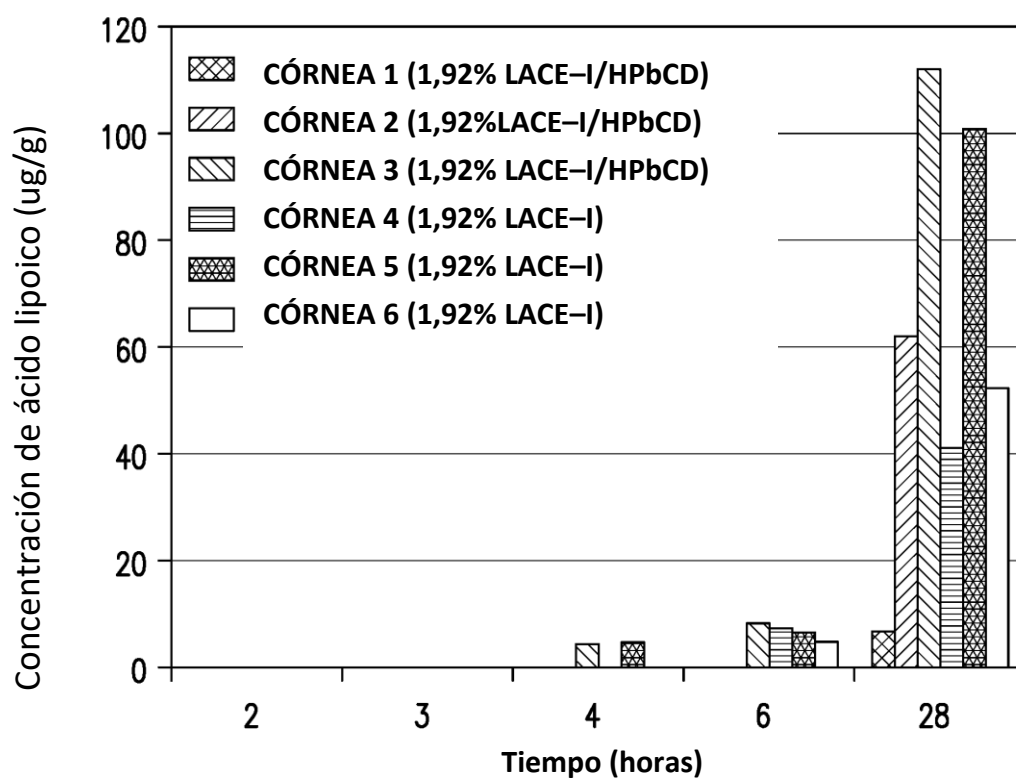


FIG.30

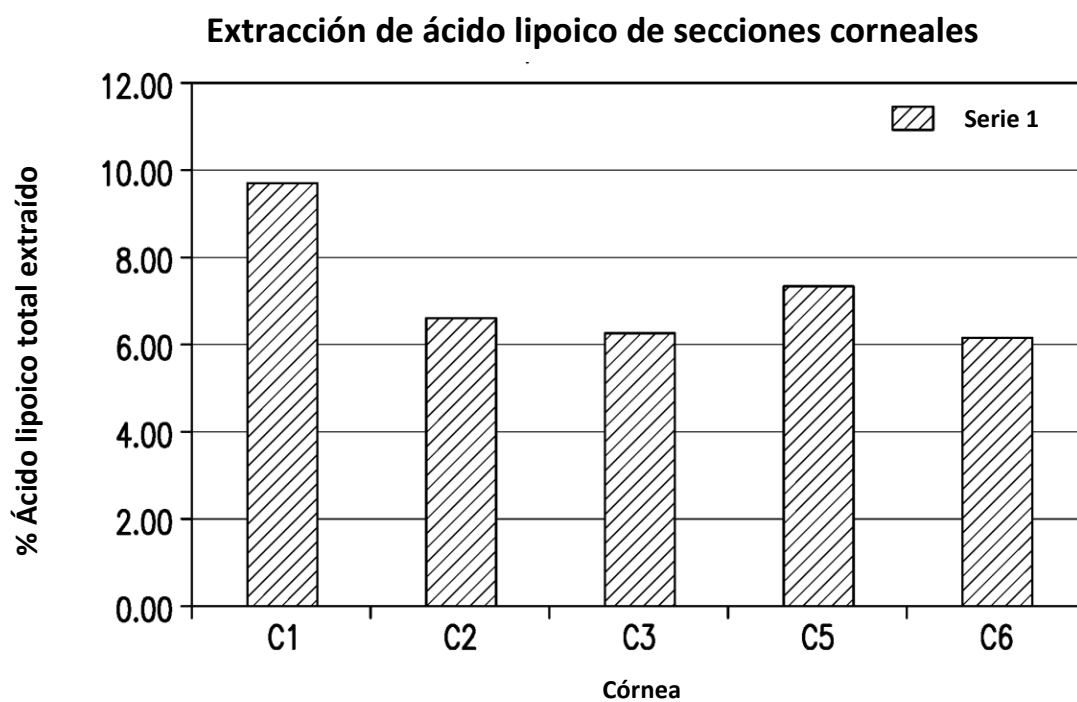


FIG.31

**Cambio en especies asociativas como una función de tiempo
en formulaciones de cantidades variables de HP-B-CD**

