



AREA ACADÉMICA DE FARMACIA

FISIOPATOLOGÍA

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DAÑO HEPÁTICO POR ALCOHOL

Protective effect of some vitamins against the toxic action of ethanol

Efecto protector de algunas vitaminas del daño tóxico por alcohol.

“



Nombre del tema: Daño hepático por alcohol

Dentro del programa de la Licenciatura en Farmacia se imparte la materia de Fisiopatología, como parte del programa de esta materia se imparte el tema de cirrosis hepática, siendo el consumo de alcohol la causa de daño por etanol.

Los alumnos obtienen el conocimiento de la fisiopatología de la cirrosis por el consumo del alcohol.



Abstract

Acute ethanol administration partially inhibits DNA and protein syntheses during liver regeneration (LR) induced by partial hepatectomy (PH) in rats. Previous findings that the magnitude of ethanol's deleterious effects on LR are related to the route and timing of its administration led us to perform studies at the ultrastructural level, comparing ethanol effects on PH-induced LR, as a consequence of its administration route. PH promoted alterations on the endoplasmic reticulum and mitochondria, accompanied by decreased glycogen and increased lipid content in cytoplasm. Structural nuclear and nucleolar activities were also evident. Intra-gastric ethanol administration practically abolished the adaptative changes found in PH-promoted regenerating hepatocytes, whereas its administration through the intraperitoneal route induced later ultrastructural modifications, indicating cellular proliferation. These results suggest that ethanol, under certain conditions, could stimulate liver proliferation triggered by PH. The mechanism underlying this surprising effect of ethanol on LR remains to be elucidated. However, it is suggested that an altered ethanol metabolism by rats subjected to PH could be involved.

KEY WORDS: alcohol; cirrosis; ethanol metabolism.



UNIVERSIDAD AUTÓNOMA DEL ESTADO DE HIDALGO

“Daño hepático por alcohol”

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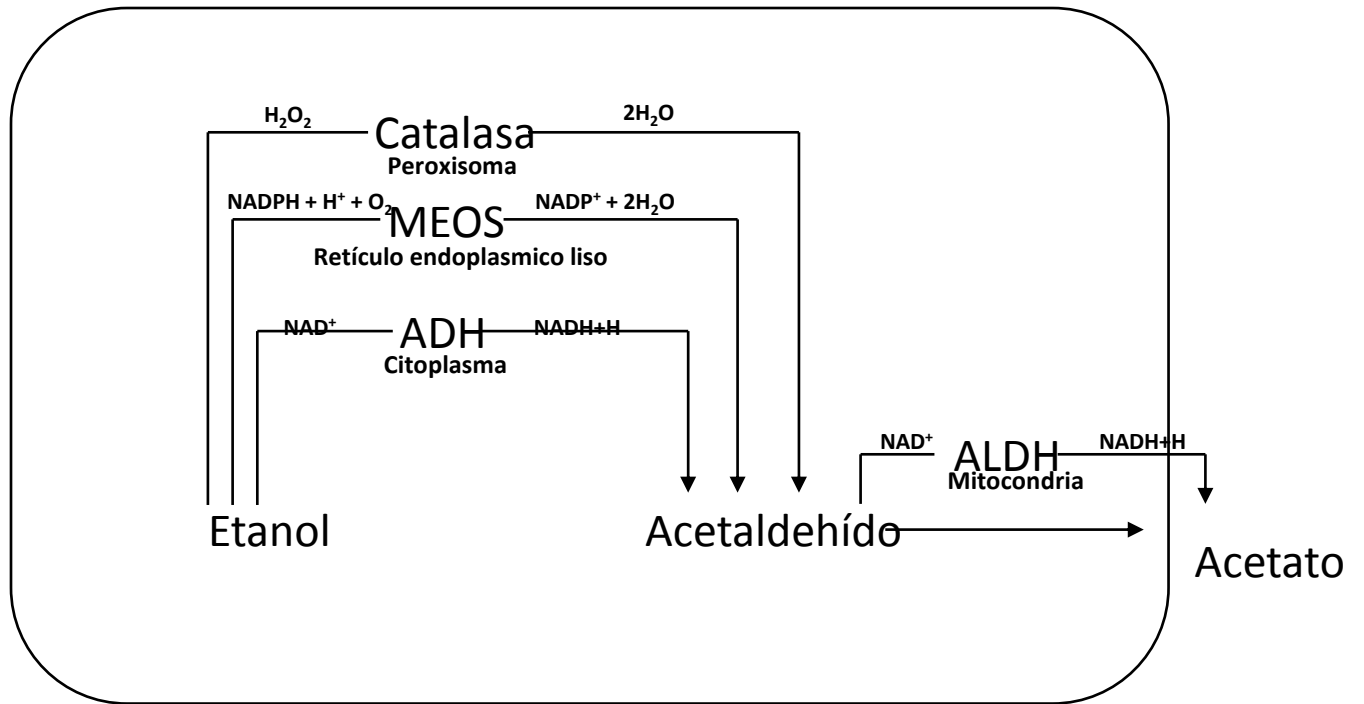
**Este es el vino que se llama octli,
que es raíz y principio de todo mal y toda perdición
porque este octli y esta borracheria
es causa de toda discordia y distensión
y de todas las revueltas
y desasosiegos de los pueblos y reinos
es como un torbellino que todo lo revuelve y
desbarata
es como una tempestad infernal
que trae consigo todos los males juntos**

Fragmento del discurso con el cual los Emperadores Aztecas, se dirigían a su pueblo inmediatamente después de su elección. (Sahagún: Historia General de las cosas de la Nueva España)



¿Qué es la vida a quien le falta el vino que
ha sido creado para contento de los hombres?
Regocijo del corazón y contento del alma
es el vino bebido a tiempo y con medida

Eclesiástico 31:27 y 28
Biblia de Jerusalén





Etanol

ADH



Acetaldehído

NAD

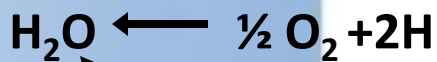
NADH + H

Citosol

Cadena respiratoria

Membrana interna mitocondrial

Matriz mitocondrial



SOD



GP



NAD

NADH + H



Acetato

ALDH

Acetaldehído



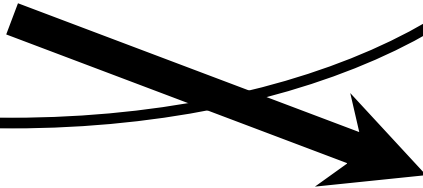


ETANOL



Hepatocito

Producción de radicales libres
y/o sustancia pro-activas



- **Daño a membranas:**
 - Lipoperoxidación
 - Perdida del potencial de acción
- **Daño a macromoléculas:**
 - Proteínas
 - Carbohidratos
 - Ácidos grasos
 - ADN
- **Alteración al balance redox**
- **Apoptosis**



Origen	Acción
Exógenos	Neutraliza el oxígeno singulete
Vitamina E	Captura radicales libres hidroxilo
Vitamina C	Captura O ₂
β-carotenos	Neutraliza peróxidos
Flavonoides, licopenos	Neutraliza el oxígeno singulete
	Captura radicales libres hidroxilo
	Captura O ₂
Endógenos enzimáticos	Regenera la forma oxidada de la vitamina E
	Neutraliza el oxígeno singulete
Superóxido dismutasa (SOD)	
Catalasa (Cat)	
Glutación peroxidasa (GPx)	
No enzimáticos	Cofactor
	Cobre, sodio, manganeso
Glutación	Hierro
Coenzima Q	Selenio
Ácido tioctico	Barreras fisiológicas que enfrenta el oxígeno a su paso desde el aire hasta las células
	Transportadores de materiales (transferrina y ceruplasmina)



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RAPID COMMUNICATION

Protective effect of some vitamins against the toxic action of ethanol on liver regeneration induced by partial hepatectomy in rats

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Table 1 Mortality and body weight parameters in each experimental group after seven days of treatment partial hepatectomy (PH), ethanol (EtOH) and some vitamins

Group	Mortality (%)	Initial body weight ¹ (g)	Final body weight ¹ (g)	Differential between final and initial weight (g)
Sham	0/30 (0)	259 ± 10	274 ± 1	15
PH	0/30 (0)	250 ± 11	267 ± 10	17
PH-EtOH	22/30 (73.3) [*]	255 ± 10	276 ± 15	21
PH-EtOH-VA	16/30 (53.3) [*]	255 ± 12	270 ± 12	15
PH-EtOH-VC	10/30 (33.3) [*]	260 ± 12	275 ± 10	15
PH-EtOH-VE	8/30 (26.6) [*]	242 ± 10	258 ± 11	16

¹Values are the mean ± SE of survivors for each experimental group ($n = 8-22$) as it corresponds. VA: vitamin A; VC: vitamin C; VE: vitamin E. ^{*} $P < 0.05$ vs the sham group; ^{*} $P < 0.05$ vs hepatectomized + ethanol group.



Table 2 Evaluation of liver regeneration parameters in each experimental group after seven days of treatment with partial hepatectomy (PH), ethanol (EtOH) and vitamins. Experimental designs are described in material and methods section

Group	Restitution liver mass ¹ (%)	Resected liver mass ¹ (g)	Final liver weight ¹ (g)	Liver/body ratio ¹ (%)	mgDNA/g liver ¹
Sham	None	None	9.41 ± 0.3	3.41 ± 0.2	2.1 ± 0.2
PH	83.95 ± 3.0	6.9 ± 0.3	8.27 ± 0.3	3.09 ± 0.3 ^a	4.1 ± 0.4 ^a
PH-EtOH	54.89 ± 2.0 ^e	6.8 ± 0.4	5.33 ± 0.2 ^c	1.93 ± 0.1 ^{ac}	2.9 ± 0.1 ^{ac}
PH-EtOH VA	62.90 ± 3.9 ^{de}	7.1 ± 0.3	6.38 ± 0.4 ^c	2.36 ± 0.3 ^{ac#}	3.4 ± 0.2 ^{ac#}
PH-EtOH-VC	79.00 ± 2.0 ^f	7.0 ± 0.5	7.90 ± 0.2 ^e	2.87 ± 0.2 ^{ab}	4.0 ± 0.3 ^{ab}
PH-EtOH-VE	81.00 ± 3.0 ^f	6.8 ± 0.2	7.86 ± 0.3 ^e	3.03 ± 0.3 ^{ab}	3.9 ± 0.4 ^{ab}

¹Values are the mean ± SE of survivors for each experimental group (n = 8-22) as it corresponds. vitamin A (VA); vitamin C (VC); vitamin E (VE). ^aP < 0.05 vs the sham group; ^eP < 0.05 vs the hepatectomized group; [#]P < 0.05 vs hepatectomized + ethanol group.



Table 3 Albumin and bilirubin levels on serum from rats after seven days of partial hepatectomy (PH) and daily ingestion of ethanol and application of vitamins A, C or E

Group	Albumin ¹ (g/dL)	Bilirubin ¹ (mg/dL)
Sham	4.5 ± 0.2	0.42 ± 0.01
PH	4.7 ± 0.3	0.40 ± 0.02
PH-EtOH	3.1 ± 0.4 ^{ac}	1.72 ± 0.04 ^{ac}
PH-EtOH VA	3.5 ± 0.3 ^{ac}	1.91 ± 0.06 ^{ac}
PH-EtOH-VC	4.2 ± 0.2 ^b	0.45 ± 0.01 ^b
PH-EtOH-VE	4.6 ± 0.3 ^b	0.29 ± 0.03 ^{ac,b}

Values are the mean ± SE of survivors for each experimental group (*n* = 8-22) as it corresponds. vitamin A (VA); vitamin C (VC); vitamin E (VE). ^a*P* < 0.05 *vs* the sham group; ^b*P* < 0.05 *vs* the hepatectomized group; ^c*P* < 0.05 *vs* hepatectomized + ethanol group.

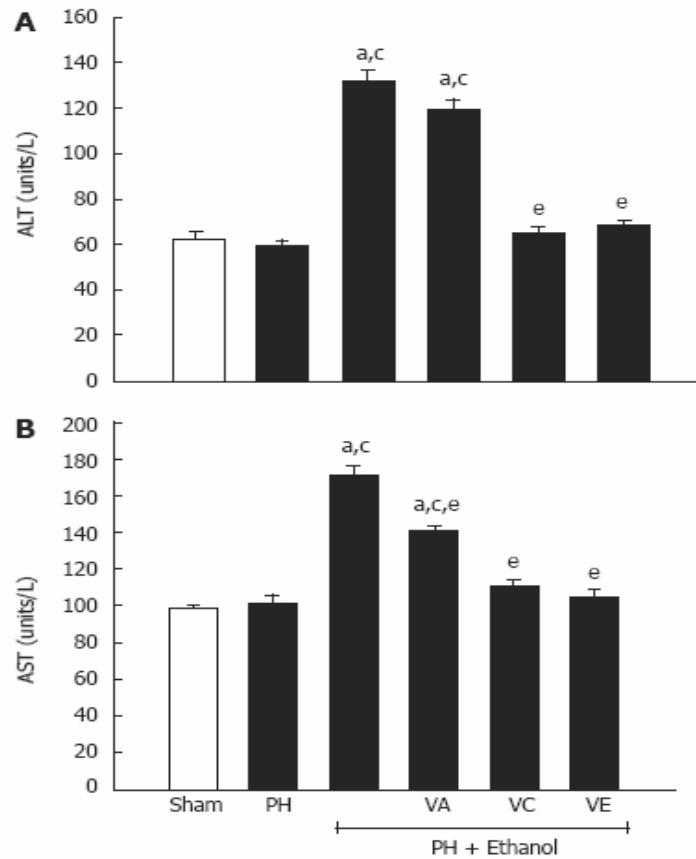


Figure 1 Effect of vitamins on specific activities of serum alanine and aspartate aminotransferase (A and B) during liver regeneration and ethanol intoxication. Values are means \pm SE ($n = 8-10$); ^a $P < 0.05$ vs the sham group (sham); ^c $P < 0.05$ vs the hepatectomized group (PH); ^e $P < 0.05$ vs hepatectomized + ethanol group (PH + Ethanol). VA: Vitamin A; VC: Vitamin C; VE: Vitamin E.

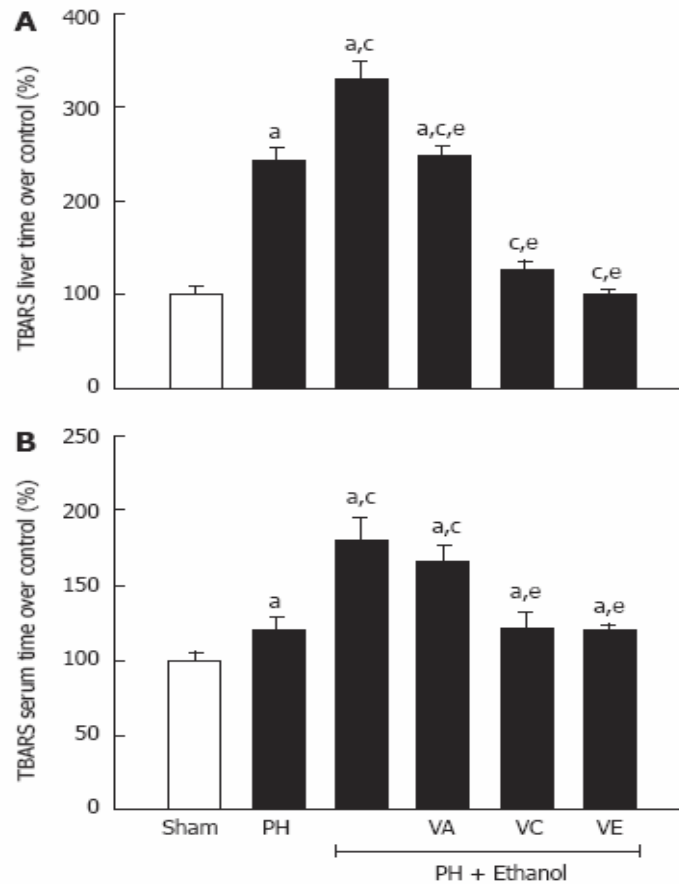


Figure 2 Effect of vitamins in both hepatic (A) and serum (B) lipid peroxidation (TBARS content) during liver regeneration and ethanol intoxication. Values are means \pm SE ($n = 8-10$); ^a $P < 0.05$ vs the sham group (sham); ^c $P < 0.05$ vs the hepatectomized group (PH); ^e $P < 0.05$ vs hepatectomized + ethanol group (PH + Ethanol). VA: Vitamin A; VC: Vitamin C; VE: Vitamin E.





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Full Length Research Paper

Hepatoprotective effects of glycine and vitamin E, during the early phase of liver regeneration in the rat

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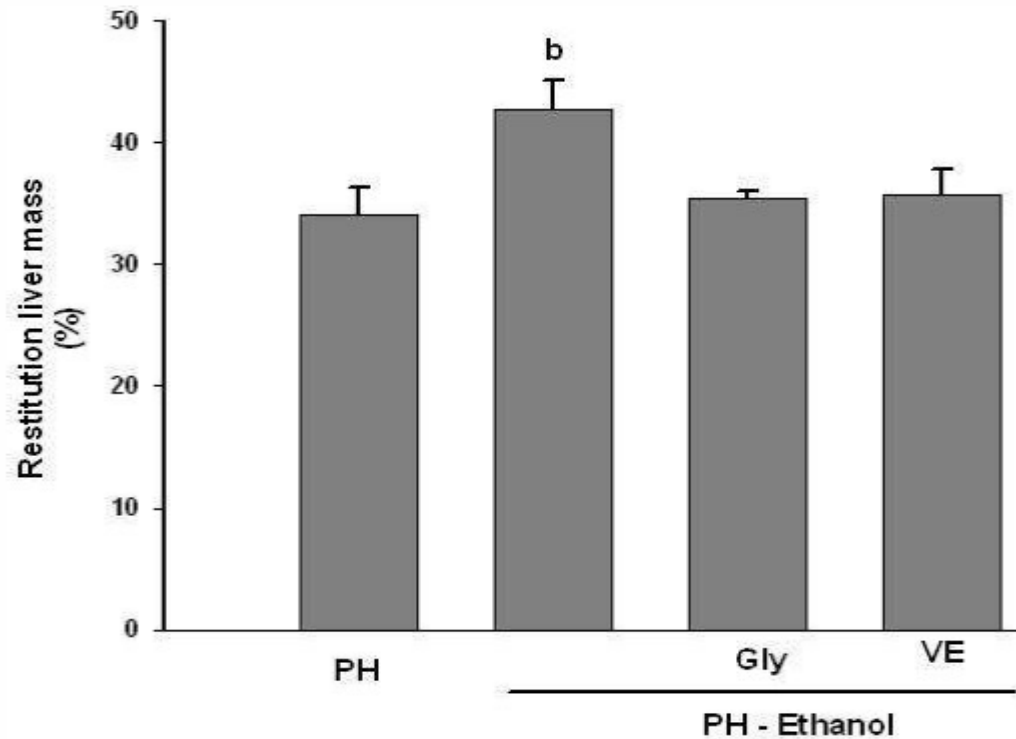


Figure 1. Effect of glycine and vitamin E on the percentage of liver-weight restitution of in rats from all ethanol-treated groups treated after partial hepatectomy. Values are means \pm standard error of mean (SE) ($n = 10$). Restitution liver mass was expressed as %. ^b $P < 0.05$ vs. the hepatectomized group (PH). PH: partial hepatectomy; Gly: glycine; VE: vitamin E.



Table 1. Albumin, bilirubin and cholesterol levels on serum from rats after of partial hepatectomy (PH) and a single administration of ethanol and application of vitamin E or Glycine.

Group	Albumin (g/dL)	Bilirubin (mg/dL)	Cholesterol (mg/dL)
Sham	3.46 ± 0.2	0.29 ± 0.2	51.8 ± 4.3
PH	3.12 ± 0.5	0.28 ± 0.1	48.0 ± 6.3
PH-EtOH	2.27 ± 0.11 ^a	0.19 ± 0.09	31.4 ± 2.1 ^a
PH-EtOH-Gly	3.56 ± 0.11 ^c	0.08 ± 0.04	51.1 ± 3.7 ^c
PH-EtOH-VE	3.39 ± 0.04 ^c	0.08 ± 0 ^c	59.1 ± 8.1 ^c

Values are the mean ± SE for each experimental group (n = 10) as it corresponds. PH: partial hepatectomy; Gly: glycine; VE: vitamin E; Sham: controls group. ^aP < 0.05 vs the sham group; ^cP < 0.05 vs hepatectomized + ethanol group

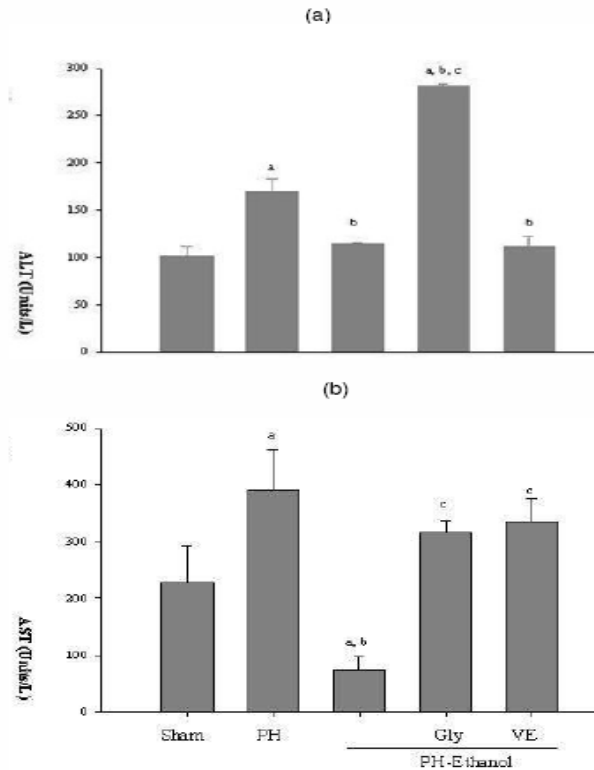


Figure 2. Effect of glycine and vitamin E on specific activities of serum alanine aminotransferase (ALT, panel A) and aspartate aminotransferase (AST, panel B) during liver regeneration and ethanol intoxication. Values are means \pm Standard error of mean (SE) (n = 10). The activity is reported in Units/L. ^aP < 0.05 vs. the sham group (sham); ^bP < 0.05 vs. the hepatectomized group (PH); ^cP < 0.05 vs. hepatectomized + ethanol group (PH-EtOH). PH: Partial hepatectomy; Gly: Glycine; VE: Vitamin E.

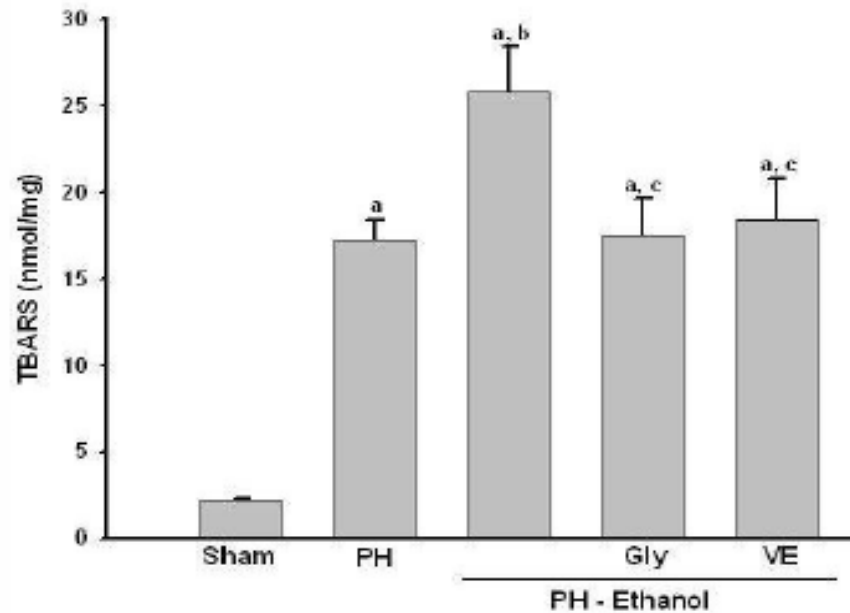


Figure 3. Effect of glycine and vitamin E on hepatic lipid peroxidation (determined as Thiobarbituric Acid Reactive Substances (TBARS) content) in all ethanol-treated groups during liver regeneration. Values are means \pm Standard error of means (SE) ($n = 10$). TBARS content is reported in nmol/mg. ^a $P < 0.05$ vs. the sham group (sham); ^b $P < 0.05$ vs. the hepatectomized group (PH); ^c $P < 0.05$ vs. the hepatectomized + ethanol group (PH-EtOH). PH: Partial hepatectomy; Gly: Glycine; VE: Vitamin E.

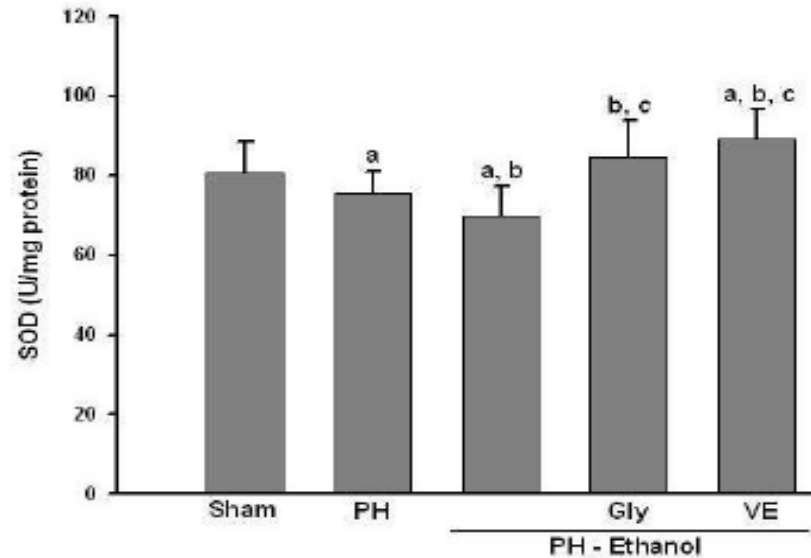


Figure 4. Effect of glycine and vitamin E on (SOD) activity in liver from all ethanol-treated groups during liver regeneration. Values are means \pm Standard error of mean (SE) (n = 10). SOD activity was expressed as U/mg protein. ^aP < 0.05 vs. the sham group (sham); ^bP < 0.05 vs. the hepatectomized group (PH); ^cP < 0.05 vs. hepatectomized + ethanol group (PH-EtOH). PH: Partial hepatectomy; Gly: Glycine; VE: Vitamin E.

Bibliografía

- Judith Parra-Vizuet, Abelardo Camacho-Luis, Eduardo Madrigal-Santillán, Mirandeli Bautista Ávila, Jaime Esquivel-Soto, Cesar Esquivel Chirino, Manuel García Luna y González Rubio, Jorge Alberto Mendoza-Pérez, Jorge Chanona-Pérez and José A. Morales-González (2009). “Hepatoprotective effects of glycine and vitamin E, during the early phase of liver regeneration in the rat”. *African Journal of Pharmacy and Pharmacology* 3:384-390. ISSN 1996-0816
- Carlett Ramírez Farías, Eduardo Madrigal-Santillán, José Gutiérrez-Salinas, Nidia Rodríguez Sánchez, Maricela Martínez Cruz, Ilse Valle Jones, Ingrid Gramlich Martínez, Alejandra Hernández-Ceruelos, and José A. Morales-González (2008). “Protective effect of some vitamins against the toxic action of ethanol on liver regeneration induced by partial hepatectomy in rats”. *World J Gastroenterol* 14:899-907. ISSN 1007-9327
- José A. Morales González. *Alcohol, alcoholismo y cirrosis. Un enfoque multidisciplinario.* (2007). 240 pp. Ed. UAEH. ISBN-970-769-117-4