

Considering the pathologic lesions of liver and changes of plasma alanine transaminase and aspartate transaminase in acetaminophen-induced toxicity in rat

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Objectives: Acetaminophen (Paracetamol) is a widely used antipyretic and analgesic drug, which in overdose can cause extensive hepatic damage. This study initiated to compare differential effects of therapeutic and toxic dose of acetaminophen on enzymatic and non-enzymatic antioxidant factors, plasma total antioxidant capacity, level of plasma AST and ALT and structure of liver in developing and adult rats. In this paper, histopathologic and enzymatic findings are report. **Methods:** 12 neonatal and 12 adult male albino Wistar rats were divided into 2 groups (neonatal and adult). In each group, the rats were randomly divided into 3 subgroups (n=4/group). Treated groups were given single low (25 mg/Kg.b.w) and high dose of APAP (450 mg/Kg.b.w), respectively. Controls received phosphate buffer salin (PBS) only as the vehicle. All animals were euthanized after 24 hours and necropsied. Tissue samples from the liver were fixed in 10% neutral buffered formalin, embedded in paraffin and sectioned at 6 microns and stained with H&E for histopathological examination. The level of plasma AST and ALT were also measured by autoanalyser. **Results:** Histopathologic examination revealed centrilobular necrosis, infiltration of inflammatory cells, swelling, granular degeneration, fatty change and single cell necrosis of hepatocytes in subgroups that received high dose of acetaminophen. Congestion, scattered foci of hepatocytes necrosis and inflammatory cell infiltration were observed in subgroups that received low dose of acetaminophen. The lesions were more severe in adult than neonatal rats. ALT in adult and ALT and AST levels in neonatal rats were significantly increased in high dose subgroups (p<0/05). **Conclusion:** The results of this study indicated that the lesions in liver were more severe in adults than neonatal rats. This can be due to inducible certain antioxidant factors and less severe induction of cytochrome P₄₅₀ in neonatal rat hepatocytes than in adults.

Key words: Acetaminophen, Hepatic necrosis, Histopathologic lesions, ALT, AST, Rat.

ALT	()	:	AST
(PBS)	()	(mg/Kg.b.w)	(mg/Kg.b.w)
%	(AST)	(ALT)	
AST ALT	ALT	(P<0.005)	P ₄₅₀
	ALT AST		

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NAPQI

NAPQI (APAP)

GSH Von Mering

.() .()

GSH

.() .()

NADP⁺ NADPH

NAPQI (Ca⁺⁺)

Ca⁺⁺ NAPQI .() ()

Mg⁺⁺ ATPase

(/ gr) (/ gr)

Ca⁺⁺ ()

DNA

.() .()

.() .()

P₄₅₀ P₄₅₀

.() .()

P N- P₄₅₀

(AST ALT) (NAPQI)

(NAPQI)

NAPQI .()

:

() ()

(±) (± g ±) .()

NAPQI

.()

(mg/Kg.b.w) (mg/Kg.b.w)

(PBS)()

4 - Blebbing

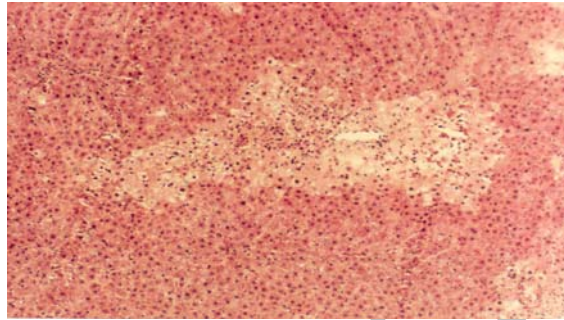
1 - N- acetyl - P- aminophenol = Paracetamol = APAP
 2 - Overdose
 3 - Safe

(°c, mM , PH =)
 (IP)
 .()
 .()
 /
 () (m/m)
 %
 ()
) () (H&E)
 .() ()
 .()
 .() (AST)
 (mg/Kg.b.w) (ALT)
 (Technicon RA-1000)
 .()
 SPSS
 .() student's t-test
 (EMH)
)
 ()
 .() ()
 :
 .()
 AST ALT (450 mg/Kg.b.w)
 ALT

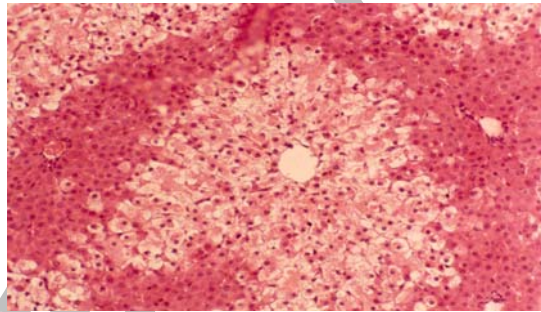
-
- 4 - Loss of nucleus
 - 5 - Midzonal
 - 6 - Cell swelling
 - 7 - Hydropic degeneration
 - 8 - Apoptosis
 - 9 - Apoptic bodies
 - 10 - Cytosegresome
 - 11 - Councilman bodies
 - 12 - Extramedullary haematopoiesis

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- 1 - Coagulative necrosis
 - 2 - Shrunken
 - 3 - Disassociated

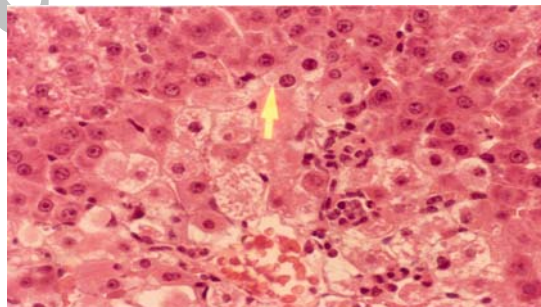
ALT (mg/Kg.b.w) APAP \pm) (P< /)
 AST mean \pm S.E.M
 P<0.05



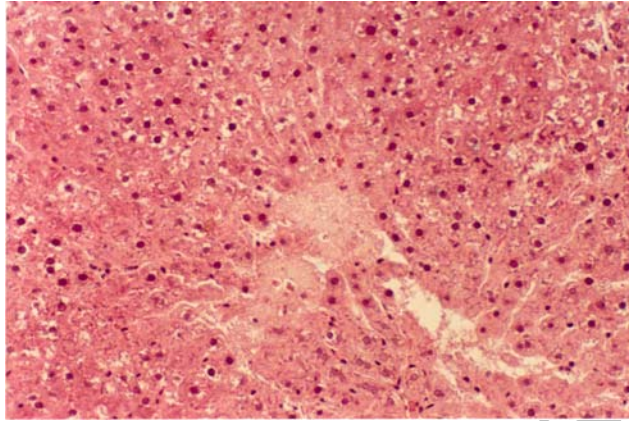
(\times H&E) (mg/Kg.b.w) (



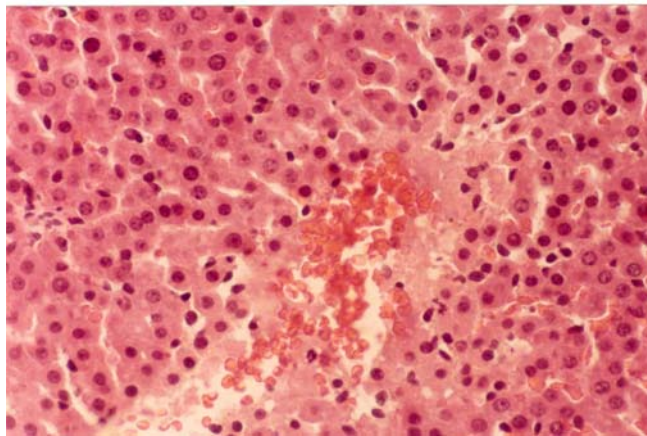
(\times H&E) (mg/Kg.b.w)



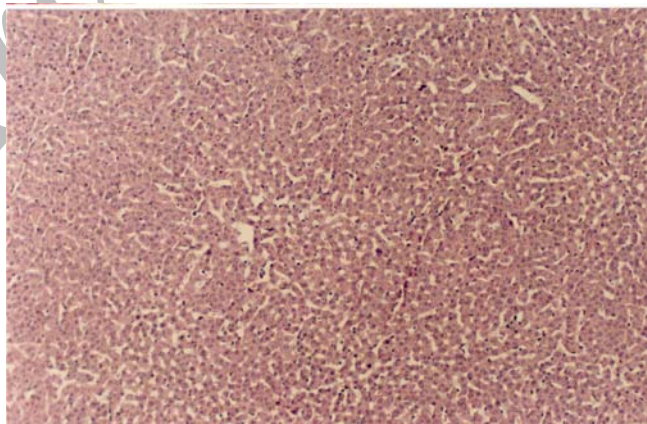
() () (\times H&E) (mg/Kg.b.w)



(× H&E) (mg/Kg.b.w)



(× H&E) (mg/Kg.b.w)



(× H&E) (

(450 mg/Kg.b.w)

AST ALT :

AST(U/L)	ALT(U/L)
c = ± /	c = ± /
t = ± *	t = ± / *
c = ±	c = ± /
t = ±	t = ± / *

c = control t = treatment * = p < /

Ray .

DNA DNA . ()

() . ()

CS . ()

Song . ()

P₄₅₀ . () ALT

(SOD))

FRAP . ()

GSH (IP) . ()

(mg/Kg.b.w)

(/)

()

mg/Kg.b.w APAP DNA

% %

()

1 - CS = Cholesteryl hemisuccinate

()

GSH

(GST)

S

NAPQI

()

N)

GSH

() P₄₅₀

(

DNA

()

Ca⁺⁺

()

Sakaue

()

(APAP)

mg/Kg.b.w

AST

DCE-

(...

- s ()

(Et-GS ipr

(SAmE)

AST

(GSH)

()

GSH

)

SAmE

()

GSH

SAmE

()

AST

ALT

()

AST

ALT

P₄₅₀

ALT

Ray

P₄₅₀

Sharma

()

()

Yunhee

mg/Kg.b.w

ICR

(mg/Kg.b.w)

()

P₄₅₀

(PCV)

BUN

()

DNA

(Hb)

()

()

()

NAPQI

Fischer 344

1 - S-Adenosylmethionine

2 - Rifampicin

3 - Moutan (Paeonia suffruticosa)

4 - ICR

()

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