# Acute Hepatotoxicity of Dentin Bonding Agents in ICR Mice

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## Objectives

There are few studies on the potential toxicity of bonding agents despite their possibility of accidental ingestion during restorative procedures. The aim of this study was to evaluate the acute hepatotoxicity of orally delivered dentin bonding agents in ICR mice.

## Methods

All five groups were prepared based on the type of the dentin bonding agents: saline(negative control), acetaminophen (500mg/kg, positive control), total-etch adhesive (TA, 5ml/kg, Scotchbond™ Multi-Purpose), self-etch adhesive (SA, 5ml/kg, Clearfil SE Bond) and universal adhesive (UA, 5ml/kg, All Bond Universal).

14 female ICR mice were randomly divided into 5 groups. Acetaminophen was dissolved in physiological saline, and all samples were dosed by intragastric gavage daily. After 7 days, all animals were sacrificed. Blood samples were obtained and the serum marker enzymes – AST (aspartate aminotransferase), ALT (alanine aminotransferase) and ALP (alkaline phosphatase) – were estimated. Liver sections from each group were prepared for histopathological analysis. Comparison of biochemical levels was carried out using one-way ANOVA ($p<0.05$).

## Results

None of the groups experienced significant elevation of the serum marker enzymes (AST, ALT, ALP) beyond the known-normal range of ICR mice. However, the histological results showed that all groups exhibited significant inflammatory changes, such as mononuclear cellular infiltration, vascular congestion, and hepatocyte swelling. Histo-pathologically, the SA and UA group expressed moderate, and the TA group expressed mild inflammatory reactions.

| Group | AST (U/L) | ALT (U/L) | ALP(U/L) |
|---|---|---|---|
| Saline (negative control) | 75.85 ± 9.83 | 24.80 ± 1.41 | 131.38 ± 41.9 |
| Acetaminophen | 84.00 ± 12.46 | 25.30 ± 7.04 | 157.23 ± 48.41 |
| Total-etch adhesive | 47.67 ± 13.69 | 27.67 ± 2.01 | 153.13 ± 9.94 |
| Self-etch adhesive | 64.10 ± 15.98 | 29.60 ± 3.11 | 130.45 ± 24.56 |
| Universal adhesive | 72.10 ± 12.06 | 33.35 ± 9.97 | 143.05 ± 31.69 |
| Normal range * | 37-134 | 14-140 | 46-291 |

**Table 1. Effects of acetaminophen, total-etch adhesive, self-etch adhesive and universal adhesive on serum marker enzyme levels.**
**Values presented are the mean ± standard deviation (*N* = 3 / group for experimental groups, 2 / group for negative control). AST: aspartate aminotransferase, ALT: alanine transaminase, ALP: alkaline phosphatase.**
*** Modified from Loeb et al (1999) (Loeb, WF and Quimby, FW. 1999. *The Clinical Chemistry of Laboratory Animals*, 2nd ed. Philadelphia: Taylor & Francis USA.)**

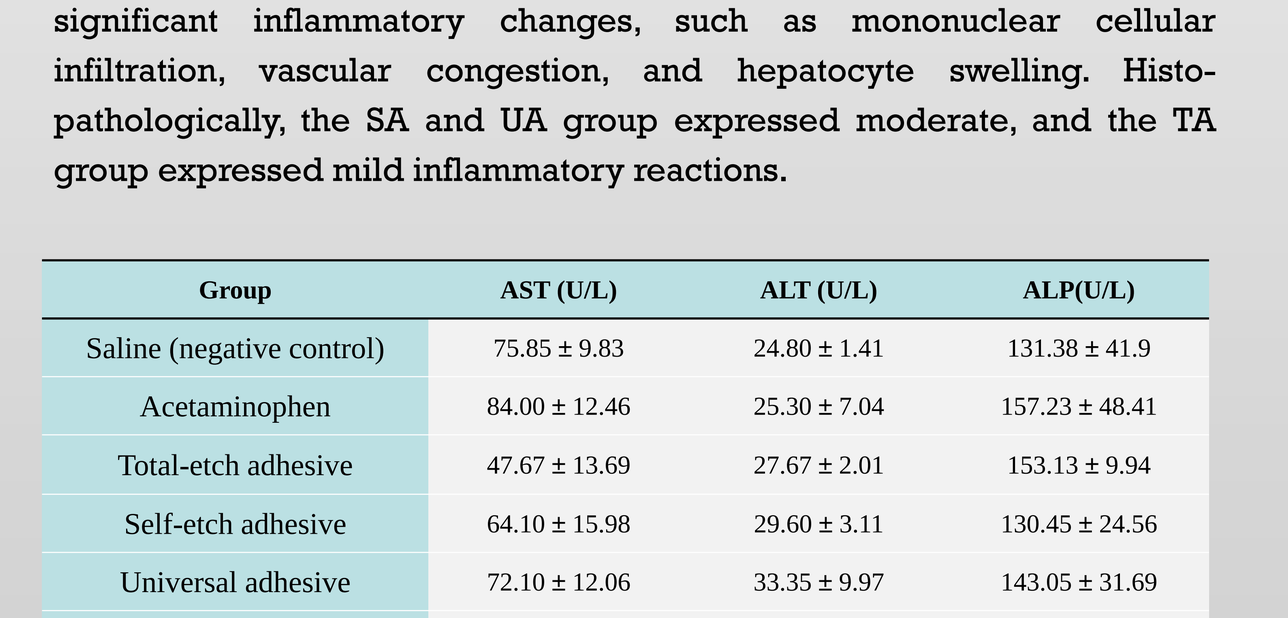


**Figure 1. Serum marker enzyme levels (AST, ALT, ALP)**

**Table 2. Histopathological inflammatory reaction grade**

| | Mononuclear cellular infiltration | Vascular congestion | Hepatocyte swelling | Score |
|---|---|---|---|---|
| Control | - | - | - | 0 |
| Acetaminophen | + | + | - | 2 |
| Total-etch adhesive | + | - | - | 1 |
| Self-etch adhesive | - | + | + | 2 |
| Universal adhesive | + | - | + | 2 |

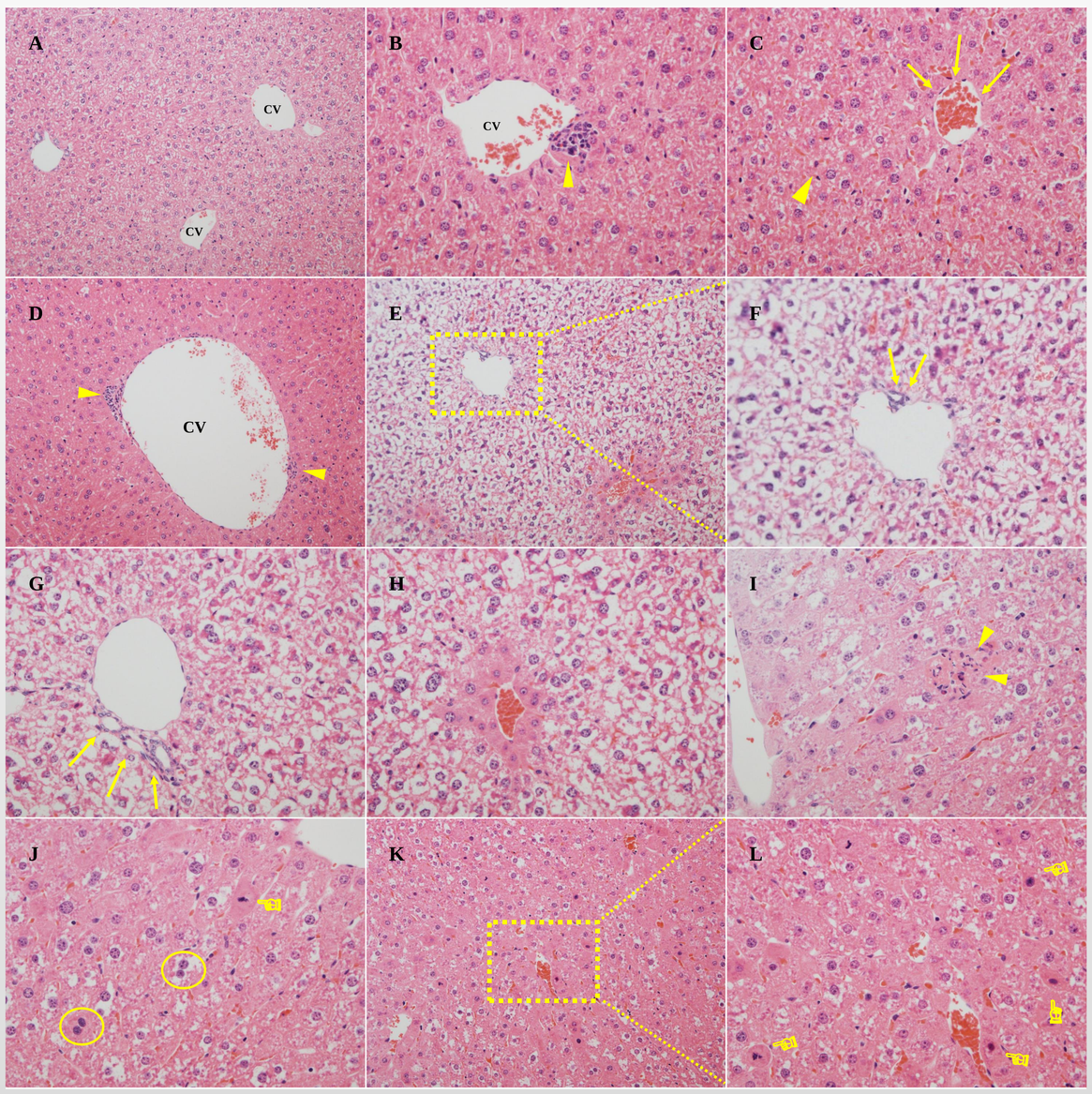


**Figure 2. Light micrographs of liver sections of mice from the different treatment groups stained with hematoxylin and eosin.**

**(a) The control mice, undamaged liver showing normal central veins and bile duct portal (x200)**
**(b-c) Treatment with acetaminophen shows (b) lymphocyte cellular infiltration(▲) around central vein(x400), (c) vascular dilatation and congestion(←), lymphocyte sinusoidal infiltration(▲) (x400).**
**(d) Treatment with total-etch adhesive shows mild mononuclear cellular infiltration(▲) around central vein (x200).**
**(e-h) Treatment with self-etch adhesive shows overall hepatocyte swelling (whitish) and (f,g) bile duct constriction(←) (e: x200, f,g: x400)**
**(i-l) Treatment with universal adhesive shows swelling of hepatocytes, (i) mononuclear cellular infiltration(▲) around diffusely necrotic hepatocytes, (j) nuclear regeneration(○) and (j,l) mitotic reaction(☜). (h,i: x400, j: x200)**

## Conclusion

The biochemical alterations of orally administrated dentin bonding agents were not significant, but histopathological findings revealed the presence of inflammatory signs of liver in all experimental groups. This suggests that the unintentional ingestion of dentin bonding agents may cause acute liver inflammation. Practitioners should take care to prevent accidental intake of bonding agents during restorative procedures.