



Acetaminophen Toxicity: A Comprehensive Review

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TABLE OF CONTENTS

INTRODUCTION	113
<i>Overview of Acetaminophen as a Widely Used Antipyretic and Analgesic</i>	113
<i>Epidemiology of Acetaminophen Poisoning</i>	113
<i>Importance of Forensic Investigation in Cases of Suspected Overdose</i>	113
<i>Aim of the Review</i>	114
I. PHARMACOKINETICS AND METABOLISM OF ACETAMINOPHEN	114
A. Normal Metabolic Pathways Involving Glucuronidation, Sulfation, and Cytochrome P450	114
B. Absorption, Distribution, Metabolism, and Excretion of Acetaminophen	114
C. Role of <i>N</i> -Acetyl- <i>p</i> -Benzoquinone Imine (NAPQI) in Hepatotoxicity	115
D. Factors Affecting Metabolism (e.g., Chronic Alcohol Use, Malnutrition, Genetic Variations) ...	115
E. Mechanism of Hepatotoxicity: NAPQI Accumulation and Glutathione Depletion	115
F. Role of Oxidative Stress and Mitochondrial Dysfunction in Liver Failure	115
II. CLINICAL FEATURES AND THE DIAGNOSTIC APPROACH	116
A. Clinical Course of Acetaminophen Toxicity	116
B. Importance of Plasma Acetaminophen Concentration and the Rumack-Matthew Nomogram ..	117
III. MANAGEMENT OF ACETAMINOPHEN POISONING	117
A. <i>N</i> -Acetylcysteine	117
B. Activated Charcoal	118
C. Methionine	119
D. Gastric Lavage	119
E. Dialysis	119
F. Liver Transplant	119
G. Management Recommendations in Accordance with the Duration of Admission to the Emergency Department	119
H. Admission Placement	119
I. Importance of Early Intervention	120

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Acetaminophen Toxicity: A Comprehensive Review

TABLE OF CONTENTS (continued)

IV. FORENSIC ASPECTS OF ACETAMINOPHEN POISONING.....	120
A. Manner of Toxicity	120
B. Autopsy Findings in Fatal Acetaminophen Toxicity	120
C. Specimen Collection for Toxicological Analysis and Postmortem Redistribution.....	121
D. Analytical Techniques.....	121
E. Interpreting Acetaminophen Concentrations	121
F. Confounding Factors in Toxicological Interpretation.....	121
G. Challenges in Forensic Differentiation from Other Hepatotoxic Agents.....	122
H. Role of Forensic Toxicologists in Legal Proceedings	122
I. Case Studies in Forensic Investigation	122
J. Public Health and Regulatory Measures	123
V. PUBLIC AWARENESS AND EDUCATION ON SAFE ACETAMINOPHEN USE.....	123
VI. REGULATORY POLICIES TO MINIMIZE OVERDOSE RISK	123
A. Pack Size Limitation.....	124
B. Maximum Packs Per Person	124
C. Minimum Age Requirement	124
D. Other Regulatory Measures	124
CONCLUSION.....	125
REFERENCES	125
ABOUT THE AUTHORS	127

REFERENCE: Menezes RG, AlMajed GA, Barnawi MA, Bubshait SM, AlAteeq RA, AlMadani RS: Acetaminophen toxicity: A comprehensive review; *Forensic Sci Rev* 38:111; 2026.

ABSTRACT: Poisoning by acetaminophen is a serious public health concern because of its accessibility and the ease with which overdoses can occur accidentally or on purpose. The liver metabolizes acetaminophen, and when taken in excess, it is transformed into a poisonous metabolite that seriously damages the liver and may result in hepatic failure and death. The cornerstone of treatment is the early administration of N-acetylcysteine, which is most effective within 8 hours of ingestion. Co-ingestants, therapy timing, and pre-existing liver diseases are some of the factors that affect toxicity. Both unintentional overdoses and deliberate poisonings have legal and forensic ramifications, especially where minors or self-harm are involved. In fatal cases, a toxicological investigation is essential to identify the cause of death and differentiate acetaminophen poisoning from other possible causes. Regulations such as age restrictions, pack-size constraints, and improved labeling have demonstrated the potential to reduce the prevalence of acetaminophen toxicity. Intentional and accidental overdoses can be avoided in part by raising public awareness and educating healthcare professionals. To lessen the impact of acetaminophen poisoning on public health systems, more research is required to enhance early identification, improve treatment techniques, and guide policy decisions. This review aims to familiarize clinicians and forensic professionals with the pharmacology, clinical presentation, management, and medicolegal aspects of acetaminophen toxicity.

KEYWORDS: Acetaminophen, acute liver injury, drug overdose, drug-related deaths, forensic toxicology, paracetamol toxicity.

38. Nourjah P, Ahmad SR, Karwoski C, Willy M: Estimates of acetaminophen (paracetamol)-associated overdoses in the United States; *Pharmacoepidemiol Drug Saf* 15:398; 2006
39. O'Malley G, O'Malley R: Acetaminophen Poisoning; *MSD Manual* (Consumer Version); Reviewed/Revised Apr. 2025, Modified Mar. 2026; <https://www.msdmanuals.com/home/injuries-and-poisoning/poisoning/acetaminophen-poisoning> (Accessed Apr. 30, 2026).
40. Pholmoo N, Bunchorntavakul C: Characteristics and outcomes of acetaminophen overdose and hepatotoxicity in Thailand; *J Clin Transl Hepatol* 7:132; 2019.
41. Prescott LF: Paracetamol (acetaminophen) poisoning: The early years; *Br J Clin Pharmacol* 90:127; 2024.
42. Price LM, Poklis A, Johnson DE: Fatal acetaminophen poisoning with evidence of subendocardial necrosis of the heart; *J Forensic Sci* 36:930; 1991.
43. Rowden AK, Norvell J, Eldridge DL, Kirk MA: Acetaminophen poisoning; *Clin Lab Med* 26:49; 2006.
44. Saudi Food and Drug Authority: Guidance for Paracetamol-Containing Oral Liquid Dosage Forms Products Intended for Pediatrics; 2022; <https://www.sfda.gov.sa/sites/default/files/2022-08/Paracetamol01.pdf> (Accessed Apr. 10, 2025).
45. Schaffer DH, Marray BP, Khazaeni B: *Acetaminophen Toxicity*; StatPearls Publishing: Treasure Island, FL; 2026; <https://pubmed.ncbi.nlm.nih.gov/28722946/> (Accessed Apr. 30, 2026).
46. Wastesson JW, Martikainen JE, Zoëga H, Schmidt M, Karlstad Ø, Pottegård A: Trends in use of paracetamol in the Nordic Countries; *Basic Clin Pharmacol Toxicol* 123:301; 2018.
47. Yan M, Huo Y, Yin S, Hu H: Mechanisms of acetaminophen-induced liver injury and its implications for therapeutic interventions; *Redox Biol* 17:274; 2018.
48. Yılmaz F: Management of paracetamol (acetaminophen) intoxication; *Eurasian J Tox* 4:17; 2022.



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