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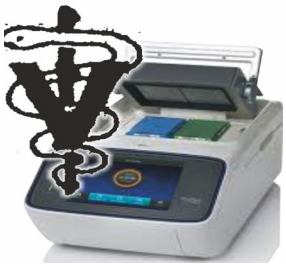

# Hepatic-induced Ascites in a Caucasian Shepherd Dog Following Chronic Paracetamol intoxication: A Case Report

Victor Eyikojonwa Amedu[1]*, Khalid Talha Biobaku[2] and Monday Onakpa[3]

[1] Postgraduate College of Veterinary Surgeons Nigeria, Medicine Faculty - Clinical Pharmacology & Toxicology Specialty.

[2]Department of Veterinary Pharmacology, University of Ilorin, Nigeria.

[3]Department of Veterinary Pharmacology, University of Abuja, Nigeria.

*Corresponding author:vicamedu.e@gmail.com Phone: +2348035670693

**Abstract**

*A 4-year-old intact male Caucasian Shepherd dog (45 kg) was presented with progressive abdominal distension, icterus and lethargy after three weeks of owner-administered human paracetamol (1000 mg BID). Clinical examination and imaging confirmed severe ascites with sonographic features of chronic hepatocellular injury and portal hypertension. Laboratory tests demonstrated marked hepatocellular enzyme elevation, hypoalbuminaemia and thrombocytopenia consistent with hepatic dysfunction. The dog received prompt antidotal and supportive therapy including intravenous N-acetylcysteine (NAC) protocol, oral silymarin, diuretics (furosemide + spironolactone), vitamin K1 and a hepatic support diet. Clinical and biochemical improvement were observed within 5–10 days and ascites resolved progressively. This report emphasises the risk of repeated over-the-counter paracetamol use in dogs, outlines practical pharmacologic management of paracetamol-induced hepatic injury and ascites, and highlights owner education and regulatory measures to prevent iatrogenic toxicities.*

**Keywords:** Paracetamol, Acetaminophen, Dog, Hepatotoxicity, Ascites, N-acetylcysteine, Caucasian Shepherd.

# Introduction

Paracetamol (acetaminophen, APA) is widely used as an analgesic and antipyretic in humans but is a well-recognised hepatotoxin in many veterinary species when given inappropriately[3]. Dogs have limited glucuronidation capacity compared with humans, predisposing them to accumulation of the reactive metabolite, N-acetyl-p-benzoquinone imine (NAPQI), glutathione depletion and centrilobular hepatic necrosis after chronic or high-dose exposure [1,6,26]. Clinical syndromes range from mild enzyme elevations to fulminant hepatic failure with secondary complications such as portal hypertension and ascites [4]. Early recognition and institution of antidotal therapy (N-acetylcysteine) and supportive care are critical to improving outcomes[4]. This case documents paracetamol-induced hepatopathy complicated by ascites in a large breed dog and details the pharmacologic rationale for the management strategy used.

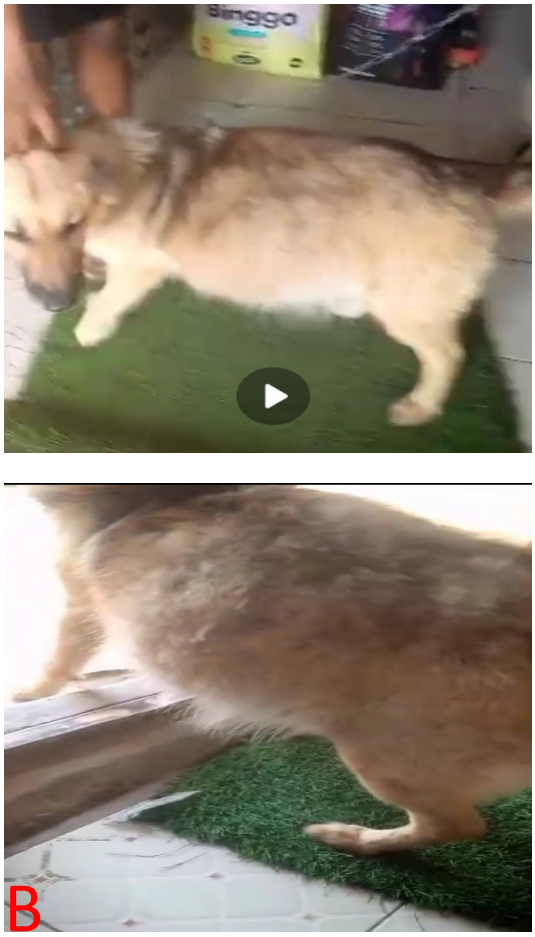


**Plate 1 A & B**: Dorso-lateral views of Caucasian Shepherd dog during physical examination

## Case presentation

### History & Signalment

A 4-year-old intact male Caucasian Shepherd dog, weight ≈45 kg, was presented with a 10-day history of progressive abdominal distension, inappetence and lethargy. The owner reported administering paracetamol 1000 mg orally twice daily for three weeks for presumed joint pain. There was no prior documented medical history.

### Clinical examination

On presentation, vital parameters were evaluated. Temperature was found to be 38.5 °C; Heart rate was 110 bpm while Respiratory rate was observed to be 30 cpm. The mucous membranes were icteric. Abdominal palpation revealed a fluid thrill and shifting dullness consistent with ascites (Plates 1A & B). Body condition score was estimated to be 4/9. Cardiorespiratory examination did not reveal clinical abnormality.

### gnostic procedures

**Blood Sample collection and analyses:** Blood samples were collected from the median cephalic vein of the dog with non-heparinized capillary tubes into Bijou bottles and allowed to clot for separation of serum. The samples were taken to Clinical pathology laboratory for liver and renal function tests as well as the full blood count.

**Liver function test:** This involved determination of liver enzyme markers (alanine transaminase, aspartate aminotransferase, gamma-glutamyl transferase, alkaline phosphatase), and

other parameters (Total protein, albumin, globulin bilirubin levels, serum albumin/globulin ratio and cholesterol). The conduct of the tests was facilitated using enzyme assay kits obtained from Randox laboratories, England and relevant spectrophotometric assays.

**Renal Function test:** Assessment of renal function in the dog was conducted to evaluate kidney function. This involved determination of serum creatinine and blood urea nitrogen (BUN), glucose, and electrolyte levels.

**Haematology:** The Packed cell volume**,** Full blood count encompassing white blood cell count, red blood cell count, differential count, platelets count, prothrombin time and Erythrocyte sedimentation rate were determined according to standard procedures.

## Laboratory results

**Table 1:** Liver function indices of dog on presentation at Day 0

| Parameter | Value | Reference Range | Interpretation |
|---|---|---|---|
| ALT | 323 IU/L | 10–100 IU/L | Marked elevation indicative of hepatocellur necrosis |
| AST | 288 IU/L | 15–66 IU/L | Elevated: liver, heart and muscle injury |
| ALP | 450 IU/L | 20–150 IU/L | Elevated: liver and bone injury |
| GGT | 58 IU/L | 0–20 IU/L | Elevated (biliary involvement) |
| Total bilirubin | 3.4 mg/dL | 0.1–0.6 mg/dL | Hyperbilirubinaemia: detoxifying function of liver compromised |
| Direct (conjugated) Bilirubin | 2.8 mg/dL | 0–0.3 mg/dL | Marked conjugated bilirubin: hyperbilirubinaemia |
| Indirect (unconjugated) Bilirubin | 0.6 mg/dL | 0–0.3 mg/dL | Mild elevation |
| Total Protein | 6.4 g/dL | 6.0–8.0 g/dL | Normal: total protein synthesis unaffected |
| Albumin | 2.1 g/dL | 2.6–4.0 g/dL | Hypoalbuminaemia |
| Globulin | 4.3 g/dL | 2.5–4.5 g/dL | Mildly elevated (reactive) |
| A/G Ratio | 0.49 | 0.8–1.5 | Reversed A/G ratio (hepatic synthetic dysfunction) |
| Cholesterol | 95 mg/dL | 110–250 mg/dL | Low (high lipid metabolism) |
| Prothrombin Time (PT) | Prolonged | 10–15 sec | Coagulopathy secondary to hepatic dysfunction |

**Key:** ALT=alanine transaminase; AST=aspartate aminotransferase; GGT= gamma-glutamyl transferase; ALP= alkaline phosphatase; A/G=albumin/globulin ratio; Reference values: Kaneko *et al.* (2008)[13]

**Table 2:** Renal function parameters of dog on presentation at Day 0

| Parameter | Value | Reference Range | Interpretation |
|---|---|---|---|
| BUN | 8.0 mg/dL | 10–26 mg/dL | Slightly reduced: kidney not damaged |
| Creatinine | 0.7 mg/dL | 0.5–1.5 mg/dL | Normal |
| Glucose | 58 mg/dL | 70–120 mg/dL | Mild hypoglycemia (kidney working optimally) |
| Electrolytes ($Na/K^+/Cl^-$) | 138/3.4/104 mmol/L | 135–150/3.5–5.5 / 98–108 | Normal sodium; mild hypokalaemia |

**Key:** BUN= Blood urea nitrogen; $Na/K^+/Cl^-$=cotransport that plays a vital role in renal salt reabsorption; Reference values: Ettinger and Feldman (2017)[8]

**Table 3:** Complete blood count of dog on presentation at Day 0

| Parameter | Value | Reference Range | Interpretation |
|---|---|---|---|
| PCV | 38% | 37–55% | Normal |
| WBC | 19.5 $\times 10^9$/L | 6–17 $\times 10^9$/L | Leukocytosis (inflammatory response) |
| Neutrophils | 84% | 60–75% | Neutrophilia |
| Lymphocytes | 12% | 12–30% | Low-normal (stress leukogram) |
| Monocytes | 3% | 2–10% | Within normal |
| Eosinophils | 1% | 0–5% | Normal |
| Platelets | 140 $\times 10^9$/L | 200–500 $\times 10^9$/L | Thrombocytopenia (suggestive of hepatic dysfunction) |
| ESR | 24 mm/hr | <15 mm/hr | Elevated (non-specific inflammatory marker) |

**Key:** PCV=Packed cell volume; WBC=White blood cell; ESR=Erythrocyte sedimentation rate; Reference values: Thrall *et al.* (2022)[29]; Feldman *et al.* (2000)[9]

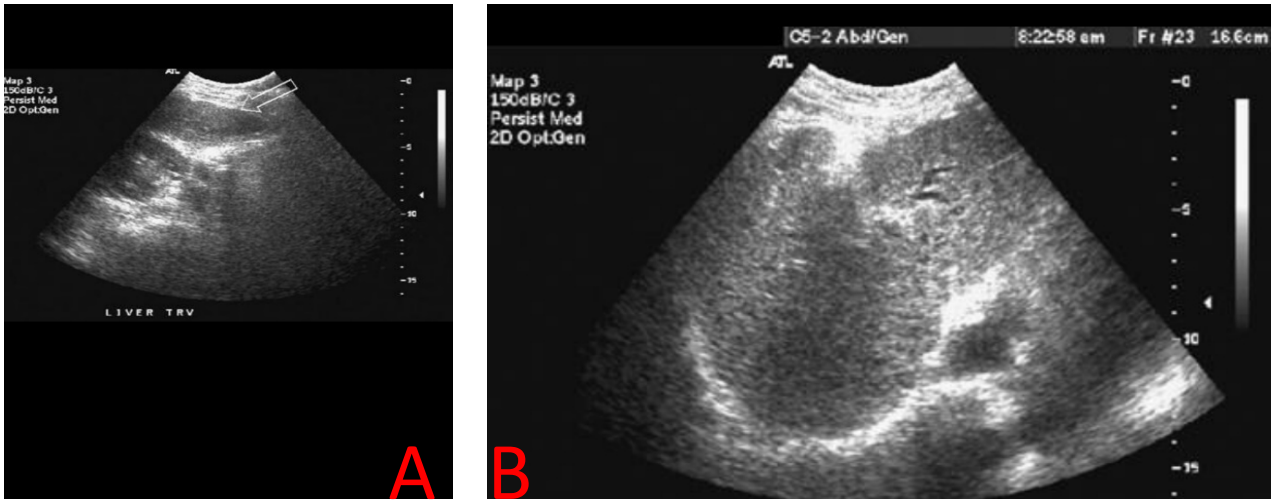


**Plate 2 A & B:** Transverse views of the liver showing irregular external contour of the left lobe (A and B in red)

**Imaging**

Abdominal ultrasonography: Imaging analysis revealed diffusely hyperechoic, reduced-sized liver with irregular margins (Plate 2 A & B); moderate anechoic peritoneal effusion consistent with ascites; mild dilation of the portal vein suggestive of portal hypertension. The gallbladder was distended with a normal wall.

**Diagnostics & differential diagnoses**

The history of the case, clinical presentation, markedly elevated liver marker enzymes particularly ALT and sonographic evidence were indicative of hepatocellular damage with portal dilatation and secondary ascites, most consistent with paracetamol-induced hepatotoxicity.

Differential diagnoses may include right-sided congestive heart failure, primary hepatic neoplasia, chronic cholangiohepatitis, or other toxic hepatic insults.

**Pharmacological Regimen/intervention**

**Immediate antidotal therapy**

- Administration of N-acetylcysteine (NAC): 140 mg/kg IV loading dose, then 70 mg/kg IV every 6 h for seven subsequent doses (total 8 doses) [23].

**Hepatoprotection & supportive pharmacotherapy**

- Silymarin (milk thistle extract): 20 mg/kg PO BID x 30 days [22].
- Livolin® Forte (1 capsule/20 kg PO q12h for 30 days) [18].
- Vitamin K1: 2.5 mg/kg SC SID × 3 days
- Hepatic prescription diet: low protein, highly digestible with antioxidant enrichment to reduce metabolic burden and aid hepatic recovery.

**Management of ascites**

- Spironolactone: 3 mg/kg PO SID × 3–7 days
- Furosemide: 2 mg/kg PO SID × 2–7 days [9,21].

**Other supportive measures**

- **Antiemetic/Prokinetic therapy:** Metoclopramide at 0.3 mg/kg IM or PO every 8 hours (TID) for 5 days
- **Fluid therapy:** A balanced isotonic crystalloid (Lactated Ringer's solution) was used at a maintenance rate of 40–60 mL/kg/day, adjusted according to hydration status, urine output, and serial electrolyte monitoring, while avoiding volume overload that could aggravate abdominal effusion [2].
- **Monitoring protocol:** Serial liver function tests (ALT, AST, ALP, total bilirubin, albumin, and total protein), renal indices (urea and creatinine), electrolytes (Na, K, Cl, $HCO_3^-$), coagulation profile (PT/aPTT), and abdominal girth were monitored to assess recovery and detect complications.

**Outcome and Follow-Up**

Progressive biochemical and hematologic improvements were observed during post-treatment and monitoring, consistent with hepatic functional recovery and resolution of systemic inflammation.

By day 14, the dog had regained full appetite and vigour, with normalization of mucous membrane coloration and resolution of icterus. Serial biochemical monitoring demonstrated near-complete hepatic recovery: ALT decreased from 323 to 95 IU/L, AST from 288 to 70 IU/L, ALP from 450 to 180 IU/L, while total bilirubin reduced from 3.4 to 0.8 mg/dL and albumin improved to 3.0 g/dL, indicating restoration of hepatic synthetic and excretory functions. Platelet count and coagulation parameters normalized concurrently, confirming improved hepatic and haematological stability (Table 4).

Although no follow-up ultrasonography was conducted, clinical and laboratory parameters collectively confirmed significant hepatic restitution. The patient was discharged on oral silymarin (20 mg/kg PO q24 h for 4 weeks) and a hepatoprotective diet [10], with scheduled outpatient reviews. Continued biochemical stability and complete clinical recovery were observed during subsequent follow-up visits.

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**Table 4:** Liver function in dog during case follow-up

| Parameter | Day 0 | Day 7 | Day 14 | Reference | Interpretation |
|---|---|---|---|---|---|
| ALT (IU/L) | 323 | 182 | 95 | 10–100 | Progressive hepatocellular recovery |
| AST (IU/L) | 288 | 150 | 70 | 15–66 | Gradual normalization |
| ALP (IU/L) | 450 | 270 | 180 | 20–150 | Decreasing cholestatic stress |
| GGT (IU/L) | 58 | 38 | 24 | 0–20 | Biliary enzyme improving |
| Total Bilirubin (mg/dL) | 3.4 | 1.8 | 0.8 | 0.1–0.6 | Excretory function restored |
| Direct Bilirubin (mg/dL) | 2.8 | 1.2 | 0.4 | 0–0.3 | Improved conjugation and excretion |
| Indirect Bilirubin (mg/dL) | 0.6 | 0.6 | 0.4 | 0–0.3 | Mild residual elevation only |
| Total Protein (g/dL) | 6.4 | 6.0 | 6.5 | 6.0–8.0 | Normal |
| Albumin (g/dL) | 2.1 | 2.5 | 3.0 | 2.6–4.0 | Synthetic function restored |
| Globulin (g/dL) | 4.3 | 3.5 | 3.5 | 2.5–4.5 | Stable |
| A/G Ratio | 0.49 | 0.71 | 0.86 | 0.8–1.5 | Improving hepatic synthesis |
| Cholesterol (mg/dL) | 95 | 118 | 156 | 110–250 | Restored hepatic synthesis |

Source of reference values: Kaneko *et al.* (2008)[13].

**Table 5:** Renal function in dog during case follow-up

| Parameter | Day 0 | Day 7 | Day 14 | Reference | Interpretation |
|---|---|---|---|---|---|
| BUN (mg/dL) | 8.0 | 10.5 | 13.0 | 10–26 | Kidney remained unaffected |
| Creatinine (mg/dL) | 0.7 | 0.8 | 0.9 | 0.5–1.5 | Stable renal function |
| Glucose (mg/dL) | 58 | 72 | 88 | 70–120 | Hepatic glycogen recovery |
| $Na^+$ (mmol/L) | 138 | 140 | 142 | 135–150 | Normal |
| $K^+$ (mmol/L) | 3.4 | 3.8 | 4.1 | 3.5–5.5 | Corrected hypokalaemia |
| $Cl^-$ (mmol/L) | 104 | 105 | 106 | 98–108 | Normal |

**Key:** $Na^+$= Sodium ion, $K^+$= Potassium ion; $Cl^-$= Chloride ion; BUN = Blood urea nitrogen; Reference values: Ettinger and Feldman (2017)[8]

**Table 6: Complete Blood Count and Coagulation Profile (Follow-up)**

| Parameter | Day 0 | Day 7 | Day 14 | Reference | Interpretation |
|---|---|---|---|---|---|
| PCV (%) | 38 | 39 | 40 | 37–55 | Normal |
| WBC ($\times 10^9$/L) | 19.5 | 13.8 | 10.6 | 6–17 | Inflammatory response resolved between day 7-14 |
| Neutrophils (%) | 84 | 75 | 68 | 60–75 | Normalized at day 7-14 |
| Lymphocytes (%) | 12 | 18 | 22 | 12–30 | Normal |
| Monocytes (%) | 3 | 4 | 5 | 2–10 | Normal |
| Eosinophils (%) | 1 | 2 | 3 | 0–5 | Normal |
| Platelets ($\times 10^9$/L) | 140 | 190 | 265 | 200–500 | Normalized at day 7-14 |
| ESR (mm/hr) | 24 | 17 | 11 | <15 | Normalized |
| PT (sec) | Prolonged (≈20) | 15 | 12.5 | 10–15 | Normalized at day 7-14 |
| aPTT (sec) | 42 | 33 | 29 | 25–35 | Normalized at day 7-14 |

**Key:** PCV=Packed cell volume; WBC=white blood cell; ESR=Erythrocyte sedimentation rate; PT=Prothrombin time; aPTT=activated partial thrromboplastin time

## Discussion

Although published toxic dose thresholds for acetaminophen in dogs are commonly above 100 mg/kg under acute exposures [3,15,19], this case described a large breed of dog exposed to a cumulative supra-therapeutic regimen (22.2 mg/kg BID for three weeks) culminating in hepatotoxicity and ascites. This suggests that chronic lower level exposure may also precipitate severe clinical outcomes in the canine species [26].

Dogs possess deficient capacity for glucuronidation of paracetamol, the primary detoxification pathway in humans [6]. This metabolic limitation shunts a high proportion of the parent drug towards the cytochrome P450 system (specifically CYP2E1), resulting in excessive formation of the highly reac-

tive intermediary metabolite, N-acetyl-p-benzoquinone imine (NAPQI). NAPQI is typically detoxified by conjugation with glutathione (GSH); however, chronic or high-dose exposure rapidly depletes hepatic GSH stores, leading to NAPQI covalently binding to hepatocellular macromolecules, resulting in centrilobular hepatic necrosis [5,6,28]. The association of drug exposure with overt clinical signs (lethargy, icterus, ascites), characteristic clinicopathological features and imaging findings provided a strong diagnostic inclination for toxic hepatopathy.

The laboratory findings confirmed both active hepatocellular injury and profound loss of hepatic synthetic function.

Hepatocellular injury markers: The significant elevations in ALT (323 IU/L) and AST (288 IU/L) are a reflection of the massive leakage of these enzymes from damaged hepatocytes, characteristic of acute necrosis.

Cholestatic and biliary markers: ALP (450 IU/L) and GGT (58 IU/L) elevations indicated concurrent cholestasis or biliary involvement, often observed in progressive hepatopathies. The marked hyperbilirubinaemia (3.4 mg/dL) was predominantly conjugated (Direct Bilirubin 2.8 mg/dL), confirming that the primary excretory function of the liver was compromised due to intrahepatic flow disruption[28].

Impaired Synthetic Function: Hypoalbuminaemia (2.1 g/dL) and the prolonged Prothrombin Time (PT) were critical markers of hepatic failure. Albumin synthesis and the production of most clotting factors are the sole functions of the hepatocyte. Their deficiency resulted in coagulopathy and reduced plasma oncotic pressure, respectively.

The development of ascites (moderate anechoic peritoneal effusion confirmed by ultrasonography) was multifactorial. The severe hypoalbuminaemia led to a drop in oncotic pressure [4], while sonographic evidence of a reduced-sized, hyperechoic liver with irregular margins and mild portal vein dilation was consistent with chronic changes and subsequent portal hypertension. Ascites formation in chronic liver failure is primarily driven by the synergy of portal hypertension (increasing hydrostatic pressure) and hypoalbuminaemia (decreasing oncotic pressure)[7,25].

Hypoglycemia (58 mg/dL) may indicate depleted glycogen reserves, impaired gluconeogenesis or active kidney function. The low BUN level of 8.0 mg/dL below the normal range of 10–26 mg/dL attested to the absence of kidney damage. The creatinine level of 0.7 mg/dL relative to the reference range of 0.5–1.5 mg/dL buttressed the functional integrity of the kidney.

The cholesterol value of 95 mg/dL out of a reference range of 110–250 mg/dL suggests that the synthetic functions of the liver were not compromised. Liver produces bile salts that aid in the emulsification of fats. Lipid (cholesterol) catabolism is supported by secretions from the liver. Thrombocytopenia with Platelet count of 140 $\times 10^9$/L (reference range: 200–500 $\times 10^9$/L) may potentially be due to impaired thrombopoietin synthesis. It is frequently linked to splenic sequestration secondary to portal hypertension [7]. The leukocytosis and neutrophilia were characteristic of a systemic inflammatory response to tissue necrosis.

The therapeutic strategy involved immediate antidote administration, stabilization of circulatory function, and aggressive management of the complications, particularly ascites and coagulopathy.

N-acetylcysteine (NAC): The cornerstone of treatment. The 140 mg/kg loading dose followed by 70 mg/kg every 6 hours for seven subsequent doses is a well-established, effective protocol adapted from human toxicology and validated in validated in veterinary practice[26]. NAC provides its therapeutic benefit via two key mechanisms: (1) as a direct precursor, it replenishes depleted glutathione stores, allowing detoxification of NAPQI; and (2) it acts as an antioxidant and

free-radical scavenger, providing direct protective effects against hepatocellular oxidative injury and promoting mitochondrial stability.

Spironolactone (Aldosterone Antagonist) + Furosemide (Loop Diuretic): This combination is the standard of care for ascites secondary to cirrhosis/portal hypertension in both human and veterinary medicine, providing a powerful synergistic diuresis while mitigating severe electrolyte derangements. Portal hypertension drives the splanchnic circulation, leading to systemic vasodilation and subsequent compensatory activation of the Renin-Angiotensin-Aldosterone System (RAAS)[7]. Spironolactone (3 mg/kg PO SID) directly counters the aldosterone-mediated sodium and water retention at the distal nephron and has potassium-sparing ability. Furosemide (2 mg/kg PO SID) was added to enhance natriuresis at the loop of Henle, accelerating fluid mobilization. The combination maximizes efficacy while minimizing the risk of diuretic-induced hypokalaemia and potential cardiorenal syndrome[21].

Vitamin K1: Administered to address the coagulopathy confirmed by prolonged PT/aPTT. Vitamin K is a crucial cofactor for the gamma-carboxylation of Vitamin K-dependent clotting factors (II, VII, IX, X). Supplementation (2.5 mg/kg SC SID) supports the production of functional clotting factors by residual viable hepatocytes [21].

Silymarin (Milk Thistle Extract): Used for its established hepatoprotective properties (20 mg/kg PO BID). Its active compound, silibinin, functions as a potent antioxidant, a membrane stabilizer, and has demonstrated antifibrotic and pro-regenerative effects in experimental models of toxic liver injury [27,30].

Livolin® **Forte (Essential p**hospholipids): The inclusion of essential phospholipids with B-complex and E vitamins was aimed at promoting hepatocyte membrane repair and stability. Analogous formulations (e.g., polyunsaturated phosphatidylcholine) have been shown in human and experimental studies to accelerate the structural and functional recovery of hepatocytes and reduce lipid peroxidation, supporting their adjunctive role in various toxic liver disorders [11,16,18, 22].

## Conclusion

This case highlights the extreme vulnerability of dogs to chronic, high-dose paracetamol exposure and provides strong diagnostic support for paracetamol-induced hepatic failure via comprehensive biochemical, haematological, and imaging analysis. The favourable outcome underscores the necessity of early and aggressive multimodal pharmacological intervention, specifically using N-acetylcysteine as the antidote [10] and judiciously combining spironolactone and furosemide for effective ascites management in the context of portal hypertension. The preventable nature of this toxicity emphasizes the critical need for owner education on the dangers of using over-the-counter human medications in veterinary species[14,15].

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