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Hydrolysis of Paracetamol in Cow Tail Broth: The Catalytic Role of Meat Matrix and Public Health Implications

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Abstract **Original Research Article**

The practice of adding paracetamol to meat during cooking to expedite tenderization is a documented but understudied food safety issue. This study investigates the interaction between paracetamol and cow tail meat during boiling, focusing on the catalytic role of the meat matrix in paracetamol hydrolysis to p-aminophenol (PAP). It also examines the optimal conditions for this conversion and the public health implications of consuming such broths. Cow tail meat was boiled with a fixed amount of paracetamol (0.1 g) and varying meat weights (0.2 – 1.2 g) to assess the extent of hydrolysis. The reverse experiment was also conducted using a fixed meat weight (1.0 g) and varying paracetamol amounts (0.1 – 1.0 g). The formation of PAP was monitored using a validated colorimetric method with p-dimethylaminobenzaldehyde (p-DMAB) at 450 nm. Control experiments with meat alone and paracetamol alone were conducted. The data were analyzed to determine the optimal meat-to-paracetamol ratio for complete hydrolysis. The study showed that the extent of paracetamol hydrolysis was directly proportional to the weight of the meat sample up to a 10:1 meat-to-paracetamol ratio, where complete conversion (100% of 0.1 g) was observed. Increasing the paracetamol concentration beyond 0.1 g in a fixed meat sample (1.0 g) resulted in a decline in absorbance, indicating incomplete hydrolysis and potential saturation of the catalytic system. Control experiments confirmed that neither the meat nor paracetamol alone produced PAP under the same conditions. The cow tail meat matrix plays a critical catalytic role in the thermal hydrolysis of paracetamol to the nephrotoxin p-aminophenol. The process is dependent on the meat-to-drug ratio, with a 10:1 ratio by weight being sufficient for complete hydrolysis of the drug. This interaction not only raises significant concerns about the potential health risks of consuming such contaminated food but also underscores the biochemical complexity of drug residues in culinary environments.

Keywords: Paracetamol; acetaminophen; chromogen; p-aminophenol; metabolite; cow tail broth.

INTRODUCTION

The culinary use of cow tail, also known as oxtail (Figure 1), is a tradition in many cultures, prized for its rich flavor and gelatinous texture when slow-cooked [1]. The unique composition of cow tail, comprising muscle, connective tissue, bone, and marrow, makes it a model for studying complex biochemical interactions during cooking [4]. The tenderization of such tough meat cuts is a process that naturally involves the breakdown of collagen and other connective tissue proteins, often facilitated by slow, moist-heat cooking [2]. However, the desire to expedite this process has led to the emergence of harmful shortcuts. A particularly alarming practice that has been reported is the use of paracetamol (acetaminophen) as a meat tenderizer [5]. Paracetamol is a widely available, inexpensive analgesic, but its application in cooking is both illegal and extremely dangerous. The rationale behind this practice is often attributed to a misunderstanding of the drug's chemical properties, with some believing it can break down meat fibers more quickly [3]. This practice is not only a form of drug misuse but also poses a significant and direct threat to public health.

Paracetamol is a well-characterized compound with a defined metabolic pathway in the human body. At therapeutic doses, it is primarily metabolized in the liver via glucuronidation and sulfation to non-toxic conjugates

[31]. A minor fraction is oxidized by cytochrome P450 enzymes (mainly CYP2E1) to form N-acetyl-p-benzoquinone imine (NAPQI), a reactive and toxic intermediate that is normally detoxified by conjugation with glutathione [30]. In cases of overdose, glutathione stores are depleted, leading to NAPQI accumulation and severe, often fatal, hepatotoxicity [6].

However, the scenario in a cooking pot is fundamentally different. The thermal and chemical environment of boiling meat can induce non-enzymatic hydrolysis of the paracetamol amide bond (Figure 2), leading to the formation of p-aminophenol (PAP) [8]. PAP is a known nephrotoxin and has been directly implicated in kidney damage in both animal models and clinical cases [7]. The potential for the meat matrix itself to act as a catalyst for this hydrolysis, through its complex mixture of proteins, amino acids, and metal ions, is a critical area of investigation that has not been fully explored. Preliminary reports have suggested that the presence of meat enhances the degradation of paracetamol but the nature and extent of this catalytic role require systematic study [9].

Figure 1: Cowtail Broth

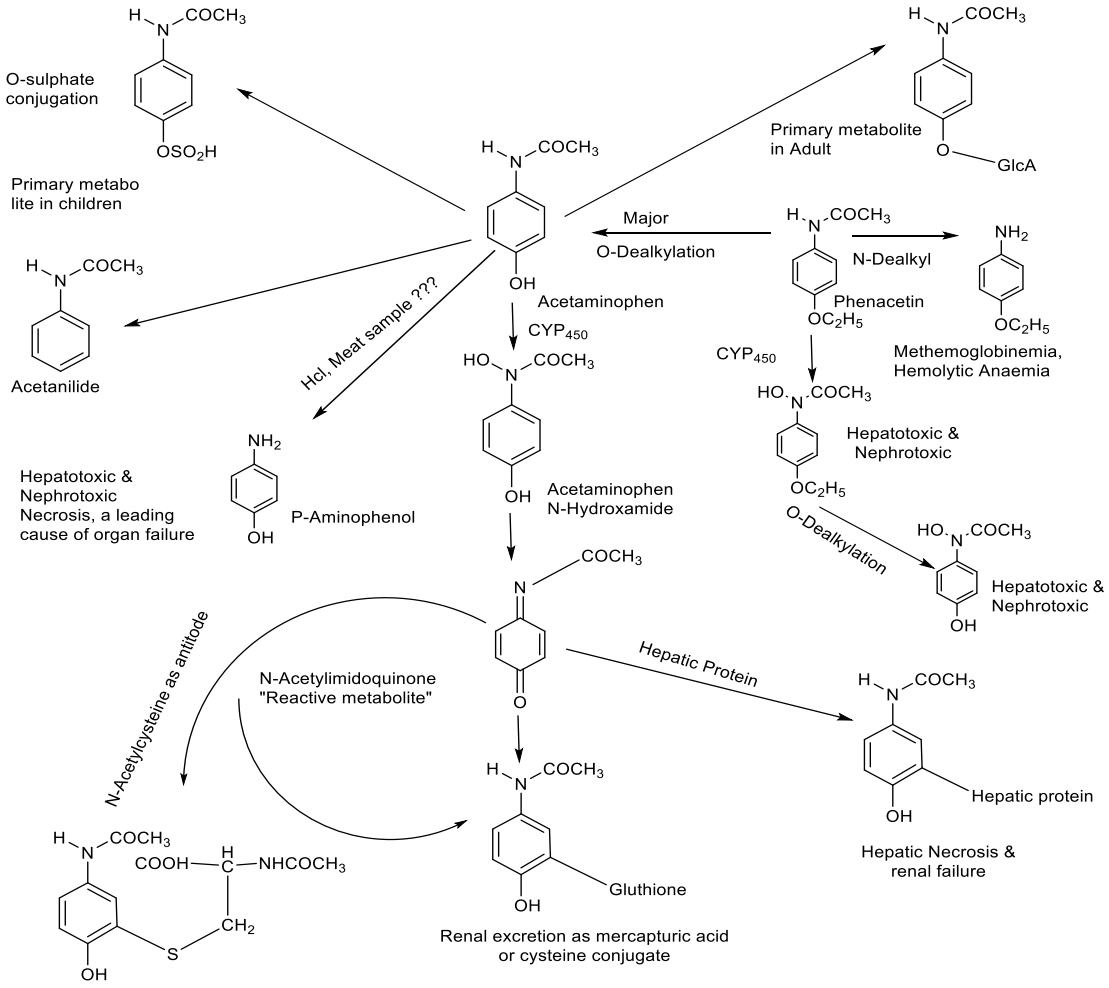

Figure 2: Metabolism of Paracetamol

Understanding the interaction between paracetamol and the meat matrix is crucial for assessing the true risk to consumers. This study aims to elucidate the catalytic role of cow tail meat in the thermal hydrolysis of paracetamol to PAP. By systematically varying the meat-to-paracetamol ratio, we sought to determine the stoichiometry of the reaction, the capacity of the meat matrix to facilitate hydrolysis, and the conditions under which complete conversion of the drug to its toxic metabolite occurs [10]. These findings are essential for providing a scientific basis for public health

warnings and for developing strategies to mitigate this dangerous practice [11].

MATERIALS AND METHODS

Fresh cow tails were obtained from a vendor at Ramat Park, Benin City, Nigeria. Paracetamol tablets (500 mg, SKG®) were purchased from a local pharmacy. All other chemicals, including p-dimethylaminobenzaldehyde (p-DMAB), ethyl acetate, and methanol, were of analytical grade and sourced from Lobachemie, India.

Study Design

Two sets of experiments were designed to assess the interaction between the meat matrix and paracetamol. All boiling experiments were conducted in 100 mL of distilled water for 4 hours, a duration representative of traditional cow tail cooking.

Meat-Weight Dependent Hydrolysis (Catalytic Role)

To investigate the catalytic effect of the meat, a fixed amount of paracetamol (0.1 g) was boiled with varying weights of cow tail meat (0.2, 0.4, 0.6, 0.8, 1.0, and 1.2 g) in separate flasks. After boiling, the mixture was extracted with ethyl acetate to isolate any PAP formed. The extract was then reacted with p-DMAB, and the absorbance was measured at 450 nm. The amount of paracetamol hydrolyzed was calculated using a pre-established calibration curve.

Drug-Concentration Dependent Hydrolysis (Simulation Study):

To assess the capacity of a fixed meat sample to hydrolyze paracetamol, a constant weight of meat (1.0 g) was boiled with increasing amounts of paracetamol (0.1, 0.2, 0.4, 0.6, 0.8, and 1.0 g) in separate flasks. The same extraction and colorimetric analysis procedure was followed to determine the extent of PAP formation. Thin Layer Chromatographic (TLC) technique was utilized to ascertain the presence of p-aminophenol, p-Dimethylaminobenzaldehyde, as well as their reaction medium [29].

Control Experiments:

Two control experiments were performed to ensure that PAP formation was dependent on the interaction of both components. The first involved boiling 1.0 g of cow tail meat in 100 mL of water without any paracetamol. The second involved boiling 1.0 g of paracetamol in 100 mL of water without any meat. Both were processed and analyzed under identical conditions.

Quantification of p-Aminophenol

The quantification of PAP was performed using the colorimetric method described in Article 1. Briefly, the ethyl acetate extract was treated with 0.2% p-DMAB in methanol, heated at 45–50°C for 10 minutes, and allowed to stand for 30 minutes. The absorbance of the resulting yellow chromogen was measured at 450 nm using a Jenway SP-800 spectrophotometer. The amount of paracetamol hydrolyzed was calculated using the Beer-Lambert equation derived from the calibration curve ($y = 0.352x + 0.0007$), where y is the absorbance and x is the amount of paracetamol hydrolyzed in grams.

Statistical Analysis

All experiments were performed in triplicate, and results are presented as mean ± standard deviation (SD). One-way analysis of variance (ANOVA) was used to analyze the significance of differences between groups, with a p-value of <0.0001 considered statistically significant.

ANALYSIS AND DISCUSSION OF RESULTS

1. **Control Experiments**

The control experiments confirmed that the formation of PAP was a result of the interaction between the meat and the drug. No color development or PAP was detected in the sample where meat was boiled alone (Table 1) or where Paracetamol was boiled alone (Table 2), demonstrating that neither component alone is capable of producing the nephrotoxic metabolite under these conditions.

Table 1: Identification of p-Aminophenol in cowtail broth using p-Dimethylaminobenzaldehyd

TEST	OBSERVATION	INFERENCE
2 mL of the cow tail broth at 2hr +2 mL Ethyl acetate + shake vigorously.	Two separate layers were formed: Ethyl acetate was above, while water remained under.	p-Aminophenol present.
2 mL of extract + little quantity of p-dimethylamino enzaldehyde + methanol + shake + heat + cool for 30min	A cloudy yellow colouration was observed	
2 mL of the cow tail broth at 2hr: 30 min +2 mL Ethyl acetate + shake vigorously.	Two separate layers were formed: Ethyl acetate was above, while water remained under.	p-Aminophenol present.
2 mL of extract + little quantity of p-dimethylamino benzaldehyde + methanol + shake + heat + cool for 30min	A yellow colour of the mixture was observed	
2 mL of the cow tail broth at 3hr +2 mL Ethyl acetate + shake vigorously.	Two separate layers were formed: Ethyl acetate was above, while water remained under.	p-Aminophenol present.
2 mL of extract + little quantity of Para-Dimethyl amino Benzaldehyde + methanol + shake + heat + cool for 30 min	A yellow colour of the mixture was observed	
2 mL of the cow tail broth at 3hr: 30 min +2 mL Ethyl acetate + shake vigorously.	Two separate layers were formed: Ethyl acetate was above while water remained under.	p-Aminophenol present.
2 mL of extract + little quantity of p-dimethylamino benzaldehyde + methanol + shake + heat + cool for 30min	A yellow colour of the mixture was observed	

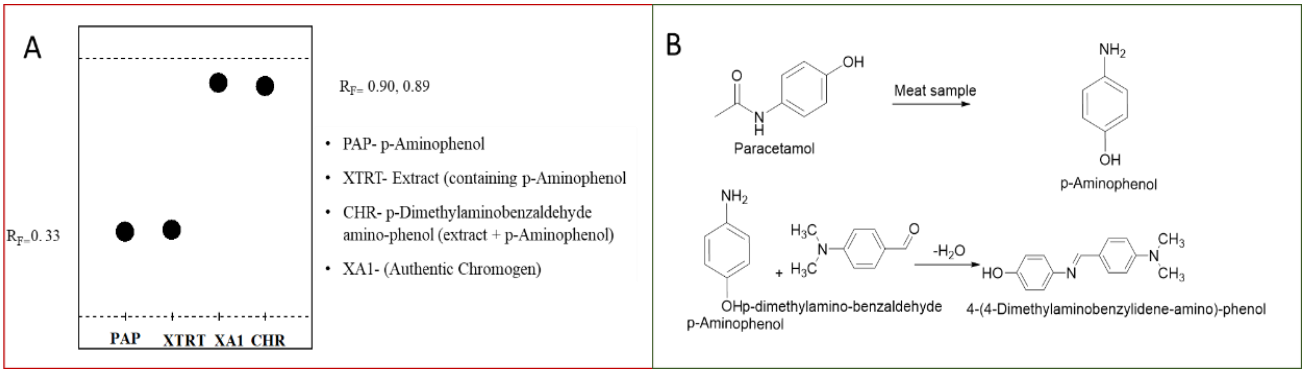

Figure 3: TLC plate of p-aminophenol using p-Dimethylaminobenzaldehyde (A). Reaction of p-aminophenol using p-dimethylamino-benzaldehyde (B)

Table 2: Boiling meat sample at various time intervals without paracetamol

TEST	OBSERVATION	INFERENCE
10 g of cowtail was weighed and boiled in 100 mL of distilled water	No observable colour changes occurred.	p- Aminophenol absent
5 mL of boiled broth for 30 min + 2 mL of 0.2% p-dimethylaminobenzaldehyde	No observable colour changes occurred.	p-Aminophenol absent
5 mL of boiled brothe for 1hr + 2mL of 2 mL of 0.2% p-dimethylaminobenzaldehyde	No observable colour changes occurred.	p- Aminophenol absent
5 mL of boiled broth for 2hr + 2 mL of 2 mL of 0.2% p-dimethylaminobenzaldehyde	No observable colour changes occurred.	p-Aminophenol absent
5 mL of boiled broth for 3hr + 2 mL of 2 mL of 0.2% p-dimethylaminobenzaldehyde	No observable colour changes occurred.	p-Aminophenol absent
5 mL of boiled broth for 4hr + 2 mL of 0.2% p-dimethylaminobenzaldehyde	No observable colour changes occurred.	p- Aminophenol absent

When paracetamol was boiled in distilled water without the presence of meat, no observable colour changes occurred throughout the different time intervals. The addition of p-dimethylaminobenzaldehyde to each boiled solution produced no visible reaction or colour development, indicating the absence of p-aminophenol. This result suggests that paracetamol alone remains stable under the experimental boiling conditions and that the decomposition to p-aminophenol requires an interaction with components present in the meat matrix.

2. Catalytic Role of Meat (Meat-Weight Dependent Hydrolysis)

The results demonstrated a clear, positive correlation between the weight of meat and the extent of paracetamol hydrolysis. As shown in Table 3, increasing the meat weight from 0.2 g to 1.0 g resulted in a proportional increase in the calculated amount of paracetamol hydrolyzed. Complete hydrolysis (0.10 g of the original 0.10 g, i.e., 100%) was achieved when the meat weight reached 1.0 g, establishing a 10:1 meat-to-paracetamol ratio as optimal for this conversion. Further increasing the meat weight to 1.2 g did not increase the amount hydrolyzed, indicating that the reaction was driven to completion.

Table 3: Absorbance at 0.1g Paracetamol and different weights of meat sample at 450 nm

Weight of Meat (g)	Mean Absorbance (± SD)	Calculated Paracetamol Hydrolyzed (g)	% Hydrolyzed
0.20	0.0063 ± 0.00082	0.016	16%
0.40	0.0123 ± 0.00125	0.033	33%
0.60	0.0183 ± 0.00082	0.050	50%
0.80	0.0239 ± 0.00082	0.066	66%
1.00	0.0359 ± 0.00082	0.100	100%
1.20	0.0359 ± 0.00125	0.100	

3. Simulation of the Meat Matrix (Drug-Concentration Dependent Hydrolysis)

When a fixed weight of meat (1.0 g) was exposed to increasing amounts of paracetamol (Table 4), a different trend emerged. At lower paracetamol loads (0.1 g and 0.2 g), the system was able to achieve complete or near-complete hydrolysis, as evidenced by the high mean absorbance (approx. 0.351). However, as the amount of paracetamol was increased to 0.4 g, the absorbance dropped sharply to 0.282, indicating that the system was becoming saturated. At the highest paracetamol load of 1.0 g, the absorbance fell to 0.072,

suggesting a significant reduction in the system's ability to hydrolyze the drug, with only a small fraction being converted to PAP.

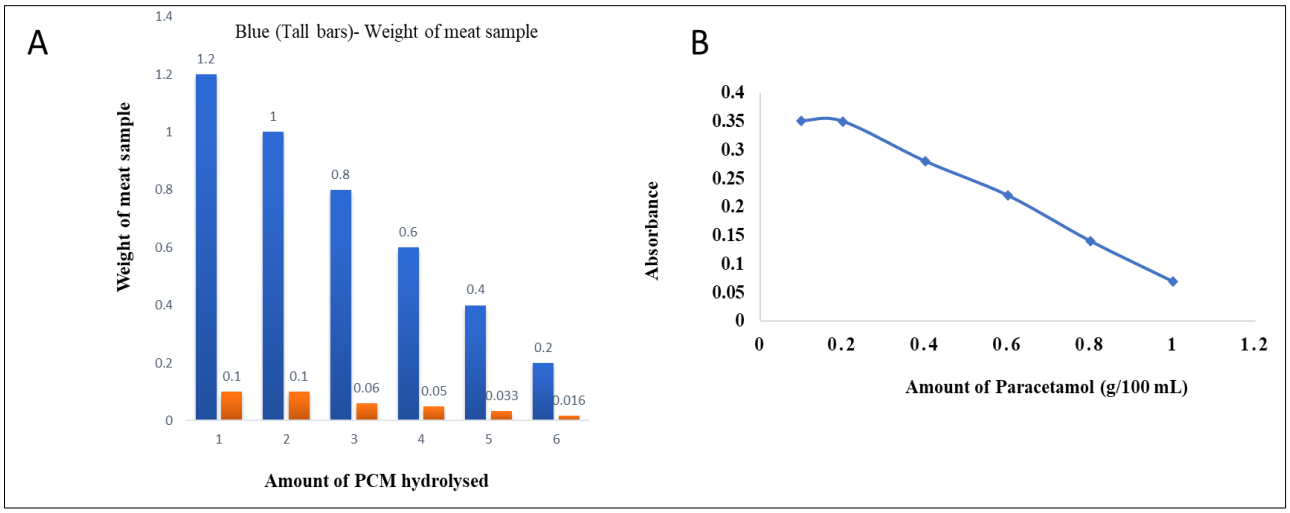

Figure 4: Bar chart showing the effect of the meat sample on paracetamol hydrolysis (A). Graph of 1.0 g meat sample and different amounts of paracetamol at 450nm (B)

Table 4: Absorbance at 1.0g meat sample and different amounts of Paracetamol at 450nm

Weight of Paracetamol (g)	Mean Absorbance (± SD)	Inference
0.1	0.351 ± 0.00082	Complete hydrolysis
0.2	0.351 ± 0.00125	Complete hydrolysis
0.4	0.282 ± 0.00125	Saturation begins
0.6	0.222 ± 0.00082	Partial hydrolysis
0.8	0.142 ± 0.00082	Partial hydrolysis
1.0	0.072 ± 0.00082	Severe saturation, minimal hydrolysis

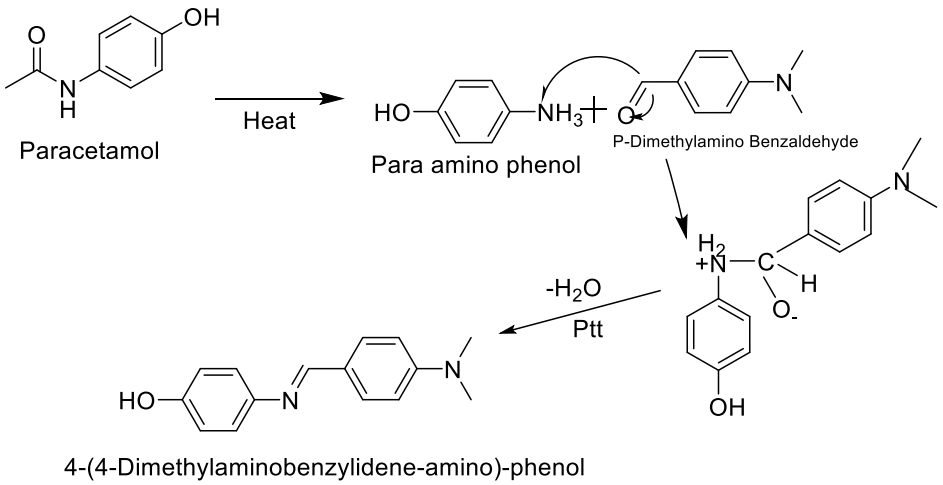

Figure 5: Reaction Mechanism of p-Dimethylaminobenzaldehyde and p-Aminophenol

DISCUSSION

This study provides the first systematic evidence that cow tail meat acts as a potent catalyst for the thermal hydrolysis of paracetamol to its nephrotoxic metabolite, p-aminophenol (PAP). The results from the control experiments are unequivocal: neither the meat matrix alone nor the paracetamol alone produced PAP under the same cooking conditions. This confirms that the observed degradation is not a simple thermal decomposition of the drug but a synergistic process requiring the complex biochemical environment of the meat. This interaction is likely mediated by components such as amino acids, metal ions (e.g., iron, zinc), and enzymes that can act as nucleophilic catalysts or provide a favorable micro-environment for amide bond cleavage [12]. The tenderizing effect of Paracetamol, which is

anecdotally reported, may be linked to the release of PAP, which could potentially interact with muscle proteins, but this remains speculative.

The meat-weight dependent hydrolysis (Table 3) clearly demonstrates a direct, linear relationship between the amount of meat and the quantity of PAP formed, up to the point of complete drug conversion. This dose-response relationship is a hallmark of a catalytic process, where the meat provides an increasing number of active sites or "catalysts" that facilitate the hydrolysis of the drug. The establishment of a 10:1 meat-to-Paracetamol ratio for complete hydrolysis is a critical finding. This ratio is highly plausible in a domestic or commercial cooking setting, meaning that if a significant amount of meat is cooked with a relatively small amount of Paracetamol, the entire dose of the drug could be converted to the toxic PAP.

The saturation study (Figure 4) provides further insight into the catalytic mechanism. The sharp decline in PAP formation when the amount of paracetamol exceeded 0.2 g in a fixed meat sample (1.0 g) indicates that the catalytic capacity of the meat is finite. Once all available catalytic sites are occupied, any additional paracetamol remains unhydrolyzed and could be present in the broth as the parent drug, which itself has toxicity risks in excessive amounts. This finding is reminiscent of enzyme kinetics, where a fixed amount of enzyme can only process a limited amount of substrate before reaching saturation. While the exact nature of the catalytic species in the meat is not identified in this study, the observed kinetic behavior strongly suggests a limited-capacity mechanism. This could involve specific metal ions or functional groups in the meat that are present in defined quantities.

The public health implications of these findings are severe. The practice of adding paracetamol to meat, even in what might be considered "small" amounts, can lead to the formation of a known nephrotoxin, PAP. The data from this study show that a typical cooking scenario (e.g., 1 kg of meat with 100 g of paracetamol) would not only result in 100% conversion of the drug to PAP but would also be well within the capacity of the meat to do so. The consumption of such meat and its broth directly expose individuals to PAP, a compound that has been linked to renal tubular necrosis and other forms of kidney damage (Newton *et al.,* 1985; Hart *et al.,* 1994; Sciskalska *et al.,* 2015). This exposure is particularly dangerous for vulnerable populations, including children and individuals with pre-existing kidney conditions.

Furthermore, this study challenges the assumption that cooking with paracetamol is simply a form of drug misuse that leads to the ingestion of the parent drug. Instead, it shows that the cooking process itself transforms the drug into a more acutely toxic metabolite. This transformation is a direct consequence of the interaction with the food matrix. The findings provide a strong scientific rationale for the public health warnings issued by agencies like NAFDAC (2020) and underscore the urgent need for public education campaigns to inform the population about the specific dangers of this practice, which go beyond the well-known risks of paracetamol overdose.

CONCLUSION

This study conclusively demonstrates that cow tail meat acts as a catalyst in the thermal hydrolysis of paracetamol to p-aminophenol, a known nephrotoxin. The catalytic effect is dependent on the meat-to-drug ratio, with a 10:1 ratio leading to complete conversion of the drug. The finite catalytic capacity of the meat matrix suggests a saturable mechanism, potentially involving specific biochemical components. These findings reveal that the use of Paracetamol in cooking is not merely a form of drug misuse but a practice that chemically transforms the drug into a more dangerous compound within the food itself. This interaction poses a significant and preventable public health risk, underscoring the critical need for enhanced regulatory enforcement and public awareness campaigns to eliminate this hazardous practice.

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