

Peer Review

# Review of: "Thermal and Packaging-Related Nanoparticles in Food: Formation Pathways, Migration Mechanisms, and Toxicological Considerations"

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Dear Authors,

Thank you for submitting your manuscript entitled " *Thermal and Packaging-Related Nanoparticles in Food: Formation Pathways, Migration Mechanisms, and Toxicological Considerations*." However, the manuscript requires further refinement before it can be considered for publication. Please find below my detailed comments and suggestions:

## A. Critical Aspects

### 1. Title

- The title is comprehensive but slightly lengthy. Consider shortening for precision, e.g., "*Nanoparticles in Food: Thermal Formation, Packaging Migration, and Toxicological Risks*." This would improve readability and indexing without losing scientific accuracy.

### 2. Abstract

- The abstract is informative but somewhat descriptive. It should be more **structured**. To improve this, phrases such as "urgent need" could be replaced with objective scientific phrasing, e.g., "There remains a need for standardized methodologies."

### 3. Introduction

- The introduction provides a strong rationale for the topic and cites relevant background.

- However, it reads more as a general overview of food contaminants than a focused lead-in to nanoparticles. The section would benefit from:
- Earlier emphasis on the **novelty of nanoparticles compared to other contaminants**.
- A clearer articulation of the **main research gap** (limited toxicological data on food-derived nanoparticles vs. engineered nanoparticles).
- The first mention of “fluorescent carbon nanoparticles” is helpful, but differentiation from carbon quantum dots (CQDs) should be expanded with structural diagrams or comparative tables.
- Clarify the gap in current literature that this study addresses.

#### 4. Discussion

- The manuscript provides an impressive breadth of studies covering multiple food types, nanoparticle types, and toxicological endpoints.

The discussion could be improved by:

- **Comparative analysis** across studies rather than reporting them sequentially. For example, grouping outcomes by food type (meat, fish, plant-based) or nanoparticle class (FDNPs vs ENPs).
- Greater critical evaluation of **dose relevance**—many animal models use unrealistically high exposures compared to typical dietary intake.
- Expanding on **mechanistic toxicology** (e.g., ROS generation, protein corona, autophagy pathways) to link nanoparticle properties with observed toxicity.

#### 5. Conclusion

The conclusion is strong but somewhat lengthy and partly repeats the discussion.

- Recommendations to consumers (gentle cooking, high-MST containers) are valuable but could be shortened or moved to a “Practical Implications” subsection.
- A sharper conclusion should highlight three take-home messages: (1) FDNPs form during high-temperature cooking, (2) ENPs migrate from packaging within regulatory limits but uncertainties persist, and (3) long-term low-dose effects remain poorly understood.

#### 6. Clarifying Questions

- Reframe to emphasize limitations and future directions (e.g., in vitro validation, cytotoxicity assays).

- Avoid definitive claims about therapeutic efficacy without experimental support. Suggest directions for **future validation studies**—e.g., testing additional scaffold types and other stem cell lines.

## 6. Clarifying Question

- I. Could the differences between food matrix effects on FDNP formation and nanoparticle migration be more quantitatively summarized?
- II. Are there attempts to compare human dietary exposure estimates to toxicological thresholds?
- III. Could the review distinguish more clearly between acute high-dose toxicity findings and chronic low-dose relevance for human health?
- IV.

## B. Technical Aspects

### i. General Technical Concerns

- **Typos and formatting:** The manuscript has minor typographical errors (e.g., inconsistent use of “fluorescent” vs. “fluorescence carbon nanoparticles”; “nanoparticle” sometimes abbreviated as NP, other times as NPs). Standardize terminology.
- **Figures and tables:** Figure 1 is useful but simplistic. Consider adding a **schematic diagram of formation and migration pathways**. Table 1 is strong, but units should be standardized (nm, mg/L,  $\mu\text{g}/\text{dm}^2$ ).
- **Grammar and style:** Some sentences are too long and complex, e.g., p.6, lines 25–32. Breaking them down would improve readability.

### ii. Page/Line Specific Suggestions

- **Page 2, lines 20–25:** The introduction to cooking and contaminants is too lengthy before mentioning nanoparticles. Suggest condensing.
- **Page 3, lines 18–22:** First mention of CNPs—add a chemical structural figure or a comparative note with CQDs.
- **Page 8, lines 10–25:** The discussion of FDNP biodistribution in pork vs. chicken is valuable; however, the text repeats “accumulation in the liver, kidney, etc.” multiple times. Consider synthesizing into a comparative table.

- **Page 13, Table 1:** Ensure consistent notation (e.g., “5.93–7.49 nm” vs. “~3.33 nm”). Use SI units consistently.
- **Pages 16–17:** The analytical methods section could be reorganized into subsections (Imaging, Spectroscopic, Separation techniques) with clearer transitions.
- **Page 19, lines 12–18:** The phrase “acute toxicity appears limited... requiring high concentrations” should be qualified with specific reference doses to improve clarity.

### Overall Recommendation

The manuscript is **highly relevant, well-researched, and timely**, but requires **minor revision** before journal acceptance. The revisions should focus on:

1. Structuring the abstract and discussion for clarity.
2. Strengthening comparative analysis across studies rather than listing results sequentially.
3. Correcting technical inconsistencies (terminology, figures, tables, grammar).
4. Adding critical analysis on dose relevance, mechanisms, and regulatory perspectives.

Once revised, this paper will make a valuable contribution to the literature on food safety and nanotechnology.

### Declarations

**Potential competing interests:** No potential competing interests to declare.