Food and Chemical Toxicology
Volume 2, Number 2, 2024

Natural Bioactive Compounds in Food: Between Therapeutic Effects and Toxicity

Joan Nita Dianti[1]

[1] Suku Dinas Kesehatan Jakarta, Jakarta, Indonesia

Article history:
Received: August 24, 2024
Revised: October 5, 2024
Accepted: November 19, 2024
Published: December 30, 2024

Keywords:
Bioactive compounds;
Dose-response;
Food safety;
Health risk;
Hormesis;
Toxicity.

Identifier:
Zera Open
Page: 122-138
https://zeraopen.com/journal/fct

Abstract

This study evaluates the dual role of natural bioactive compounds in food consumption, focusing on their therapeutic benefits, dose-dependent effects, and potential toxicity. Using a qualitative Systematic Literature Review (SLR) approach, this study synthesizes recent evidence to examine how natural compounds influence human health through complex biological mechanisms. The findings indicate that bioactive compounds contribute to health promotion through antioxidant and anti-inflammatory effects, but their impact is strongly dependent on dosage and exposure conditions. The concept of hormesis highlights that low doses may produce beneficial effects, whereas higher doses can lead to toxicity. In addition, natural compounds may induce adverse outcomes such as hepatotoxicity and oxidative imbalance when consumed in excessive amounts or under improper conditions. This study emphasizes that natural origin does not guarantee safety and highlights the need for integrative risk assessment approaches that consider dose-response relationships and long-term exposure.

1. Introduction

Natural bioactive compounds present in food have gained considerable attention due to their potential role in promoting human health and preventing disease. These compounds, including polyphenols, flavonoids, and other phytochemicals, are widely recognized for their antioxidant, anti-inflammatory, and therapeutic properties, making them an integral component of functional foods and modern dietary strategies (Martirosyan et al., 2022). A growing body of research highlights the beneficial effects of these compounds in reducing the risk of chronic diseases such as cardiovascular disorders, metabolic conditions, and certain cancers. As noted by Teodoro (2019), bioactive compounds contribute to health promotion through their ability to modulate cellular processes and protect against oxidative damage.

However, the increasing use and consumption of natural compounds have also raised concerns regarding their safety and potential toxicity. While often perceived as inherently safe due to their natural origin, evidence suggests that these compounds may exert adverse effects under certain conditions, particularly when consumed in high doses or in concentrated forms (Vilas-Boas et al., 2021). One of the key concepts explaining this dual nature is hormesis, which describes a biphasic dose–response relationship where low doses of a substance may produce beneficial effects, while higher doses result in toxicity. Experimental evidence has demonstrated that phytochemicals can exhibit such dose-dependent behavior, challenging the conventional assumption that natural compounds are uniformly beneficial (Jodynis-Liebert & Kujawska, 2020).

The concept of hormesis has been further supported by studies showing that bioactive compounds can induce adaptive cellular responses that enhance resilience at low exposure levels. Butterfield et al. (2023) emphasize that these adaptive responses are closely linked to cellular stress mechanisms, which can shift from protective to harmful depending on exposure intensity. In addition to dose-dependent effects, natural compounds may also interact with biological systems in ways that lead to unintended toxic outcomes. Herbal products, for example, have been associated with hepatotoxicity and adverse drug interactions, highlighting the need for careful evaluation of their safety profiles (Parvez & Rishi, 2019).

Recent reviews have further documented cases of toxicity associated with traditional and herbal medicines, indicating that the use of plant-based compounds is not without risk. Philips and Theruvath (2024) report that certain herbal substances can induce liver injury and other adverse effects, particularly when used without proper regulation or dosage control. At the mechanistic level, the effects of natural compounds are often mediated through oxidative stress and redox signaling pathways. While antioxidants are generally considered protective, their activity can also contribute to pro-oxidant effects under specific conditions, leading to cellular damage and dysfunction (Zahra et al., 2021).

This dual role of oxidative processes highlights the complexity of evaluating the health impact of natural compounds. Jomova et al. (2023) suggest that reactive oxygen species can act as both signaling molecules and mediators of toxicity, depending on the balance between production and antioxidant defense systems. Despite extensive research on the beneficial properties of natural compounds, many

studies focus predominantly on their positive effects without adequately addressing potential risks. This imbalance in the literature may contribute to misconceptions regarding the safety of natural products and limit the effectiveness of risk assessment approaches.

Therefore, there is a need for a more balanced and integrative perspective that considers both the therapeutic benefits and toxicological risks of natural bioactive compounds. Such an approach is essential for understanding their role within food systems and for developing appropriate safety guidelines. This study aims to evaluate the dual role of natural bioactive compounds in food consumption by synthesizing evidence on their beneficial effects, dose-dependent responses, and potential toxicity. Using a qualitative Systematic Literature Review (SLR) approach, this study seeks to provide a comprehensive framework for assessing the safety and health implications of natural compounds in modern diets.

2. Literature Review

2.1. Bioactive Compounds and Their Functional Role in Food

Natural bioactive compounds are widely distributed in plant-based foods and are increasingly incorporated into modern diets due to their potential health benefits. These compounds, including polyphenols, flavonoids, and other phytochemicals, play a significant role in functional foods by contributing to antioxidant activity and metabolic regulation. Martirosyan et al. (2022) emphasize that bioactive compounds are essential components of functional food science due to their ability to influence physiological processes and support disease prevention.

In addition to their nutritional value, bioactive compounds are used in food preservation and safety applications, where they serve as natural alternatives to synthetic additives. Ferreira et al. (2021) highlight that these compounds can enhance food stability and extend shelf life while also providing health-related benefits. This dual functionality has contributed to their widespread use in food systems.

2.2. Dose-Response Relationship and Hormesis

The effects of natural bioactive compounds are not uniform and are strongly influenced by dose and exposure conditions. The concept of hormesis describes a biphasic response in which low doses of a compound produce beneficial effects, while higher doses may lead to toxicity. Experimental studies have demonstrated that phytochemicals can exhibit such dose-dependent behavior, challenging the assumption that natural compounds are inherently safe (Jodynis-Liebert & Kujawska, 2020). Hormetic responses are often associated with adaptive cellular mechanisms that enhance resilience to stress. Butterfield et al. (2023) explain that low-level exposure to bioactive compounds can activate protective pathways, including antioxidant defenses and stress response systems. However, when exposure exceeds certain thresholds, these adaptive mechanisms may be overwhelmed, resulting in harmful effects.

Further evidence suggests that biphasic responses are not limited to specific compounds but may represent a general characteristic of many natural substances. Nie et al. (2023) demonstrate that anti-inflammatory responses can vary depending on dosage, reinforcing the importance of dose consideration in evaluating health outcomes.

2.3. Toxicity of Natural and Herbal Compounds

Despite their beneficial properties, natural compounds can also pose health risks, particularly when consumed in excessive amounts or under inappropriate conditions. Herbal products, which are often perceived as safe due to their natural origin, have been associated with various adverse effects. Parvez and Rishi (2019) highlight that herb–drug interactions and toxicity represent significant concerns in the use of plant-based products.

Recent studies have documented cases of hepatotoxicity linked to herbal compounds, indicating that certain natural substances can cause liver damage. Philips and Theruvath (2024) report that the use of herbal medicines without proper regulation or dosage control can lead to serious health consequences. These findings challenge the common perception that natural products are inherently safe. In addition to direct toxicity, the safety of natural compounds may be influenced by factors such as contamination, processing, and formulation. van Wyk and Prinsloo (2020) emphasize that variability in composition and quality can contribute to unpredictable health effects, further complicating risk assessment.

2.4. Mechanisms of Action: Oxidative Stress and Biological Interaction

The biological effects of natural compounds are closely linked to their interaction with oxidative stress pathways and cellular signaling mechanisms. Antioxidants are generally recognized for their ability to neutralize reactive oxygen species and protect against cellular damage. However, under certain conditions, these compounds may also exhibit pro-oxidant activity, leading to adverse effects (Zahra et al., 2021).

Reactive oxygen species play a dual role in biological systems, functioning as both signaling molecules and mediators of toxicity. Jomova et al. (2023) explain that the balance between oxidative stress and antioxidant defense is critical in determining health outcomes. Disruption of this balance may contribute to the development of chronic diseases. The complexity of these mechanisms is further highlighted by the interaction between natural compounds and cellular pathways. Unsal et al. (2021) note that oxidative stress responses can vary depending on the type of compound and the physiological context, underscoring the need for a nuanced understanding of their effects.

2.5. Risk Assessment and Safety Considerations

The evaluation of natural bioactive compounds presents unique challenges for risk assessment due to their dual role as both beneficial and potentially harmful substances. Traditional toxicological approaches often focus on identifying harmful effects at high doses, but may not fully capture the complexity of dose-dependent responses and long-term exposure.

Recent studies emphasize the need for more comprehensive frameworks that integrate both beneficial and adverse effects in evaluating the safety of natural compounds. Vilas-Boas et al. (2021) highlight that safety assessments should consider factors such as dosage, exposure duration, and interactions with other compounds. Overall, the literature indicates that the health impact of natural bioactive compounds cannot be understood through a simplistic beneficial-versus-harmful dichotomy. Instead, a more integrative approach is required to account for

their complex biological interactions and dose-dependent effects within food systems.

3. Methods

This study employs a qualitative Systematic Literature Review (SLR) approach to evaluate the dual role of natural bioactive compounds in food consumption, with a focus on their therapeutic effects, dose-dependent responses, and potential toxicity. The SLR method is used to systematically synthesize existing scientific evidence from multiple disciplines, including food science, toxicology, pharmacology, and public health, without generating new experimental data. The literature search was conducted using academic databases and publisher platforms. The search strategy utilized combinations of keywords such as "bioactive compounds," "natural products," "phytochemicals," "hormesis," "dose-response," "herbal toxicity," and "oxidative stress" to identify relevant studies addressing both beneficial and adverse effects of natural compounds.

The inclusion criteria were limited to peer-reviewed articles published between 2019 and 2024 to ensure alignment with recent developments in functional food research and toxicological evaluation. Studies were selected based on their relevance to natural compounds in food systems, including those examining functional properties, dose-dependent effects, toxicity, and biological mechanisms. Studies focusing exclusively on plant physiology without relevance to human health were excluded.

The selected literature was analyzed using qualitative thematic synthesis, which involved identifying recurring patterns, conceptual relationships, and convergent findings across studies. The analysis was structured around key thematic areas, including functional roles of bioactive compounds, hormesis and dose-response relationships, toxicity of herbal products, oxidative stress mechanisms, and challenges in risk assessment. Rather than applying quantitative meta-analysis, this study emphasizes conceptual integration to provide a comprehensive understanding of the balance between therapeutic effects and toxicity of natural bioactive compounds in food systems.

4. Results

This section presents the synthesized findings on natural bioactive compounds in food systems, focusing on their functional benefits, dose-dependent responses, toxicity risks, and underlying biological mechanisms. The results highlight that these compounds exhibit a dual role in human health, where beneficial effects are closely linked to dosage, exposure conditions, and biological interactions.

4.1. Functional Benefits and Applications of Bioactive Compounds

The findings show that natural bioactive compounds are widely recognized for their beneficial effects on human health, particularly in the prevention and management of chronic diseases. These compounds contribute to antioxidant activity, modulation of metabolic pathways, and regulation of inflammatory responses, supporting their role in functional foods (Martirosyan et al., 2022).

In addition to their physiological benefits, bioactive compounds are increasingly used in food systems for preservation and safety purposes. Ferreira et al. (2021) indicate that these compounds can enhance food quality and stability, providing a natural alternative to synthetic additives while maintaining nutritional value. However, the beneficial effects of these compounds are not uniform and depend on multiple factors, including dosage, bioavailability, and individual physiological conditions. This variability highlights the complexity of evaluating their role in food systems.

Table 1. Functional Benefits and Potential Risks of Natural Bioactive Compounds

Category	Functional Role	Beneficial Effect	Potential Risk
Antioxidants	Neutralization of reactive species	Protection against oxidative damage	Pro-oxidant activity at high doses
Anti-inflammatory compounds	Regulation of immune response	Reduction of inflammation	Disruption of normal signaling pathways
Phytochemicals	Modulation of metabolic processes	Disease prevention support	Toxicity at excessive intake
Herbal compounds	Therapeutic applications	Alternative treatment options	Adverse effects and toxicity

4.2. Dose-Dependent Effects and Hormesis

The results demonstrate that the effects of natural compounds are strongly influenced by dose, with many compounds exhibiting hormetic behavior. Low levels of exposure are associated with beneficial effects, while higher levels may lead to toxicity. Experimental evidence confirms that phytochemicals can induce biphasic dose–response patterns, supporting the concept of hormesis (Jodynis-Liebert &

Kujawska, 2020). This dose-dependent behavior is linked to adaptive cellular responses that enhance resilience under mild stress conditions. Butterfield et al. (2023) explain that these responses involve activation of protective pathways, including antioxidant systems and stress-response mechanisms.

At higher exposure levels, these protective mechanisms may become insufficient, resulting in adverse effects. Nie et al. (2023) further demonstrate that anti-inflammatory responses can shift toward harmful outcomes when exposure exceeds optimal levels, emphasizing the importance of dosage in determining health impact.

4.3. Toxicity of Natural and Herbal Compounds

The findings indicate that natural compounds can pose significant health risks under certain conditions, particularly when consumed in high doses or without proper regulation. Herbal products, which are widely used for therapeutic purposes, have been associated with adverse effects such as hepatotoxicity and interactions with pharmaceutical drugs (Parvez & Rishi, 2019). Recent evidence highlights that cases of toxicity related to herbal medicines are not uncommon, particularly in contexts where quality control and dosage regulation are lacking. Philips and Theruvath (2024) report that certain herbal substances can lead to liver injury and other serious health outcomes.

Variability in composition, contamination, and processing methods further contributes to the unpredictability of natural compound safety. van Wyk and Prinsloo (2020) emphasize that these factors can significantly influence the toxicity profile of plant-based products.

4.4. Mechanisms of Action and Biological Interaction

he biological effects of natural compounds are mediated through complex interactions with cellular and molecular pathways. Oxidative stress plays a central role in these processes, as many bioactive compounds interact with reactive oxygen species and influence redox balance within cells (Zahra et al., 2021). Reactive oxygen species can function as both beneficial signaling molecules and harmful agents, depending on their concentration and context. Jomova et al. (2023) highlight that this dual role is critical in understanding how natural compounds can produce both protective and toxic effects.

The interaction between natural compounds and cellular systems is further influenced by factors such as metabolic pathways, exposure duration, and individual variability. Unsal et al. (2021) note that these interactions contribute to the complexity of predicting health outcomes associated with bioactive compound consumption.

Table 2. Integrated Framework of Natural Compound Effects and Health Risks

Process Stage	Description	Mechanism	Health Outcome
Dietary intake	Consumption of bioactive compounds	Variable exposure levels	Initial physiological interaction
Cellular response	Interaction with biological systems	Oxidative stress and signaling pathways	Adaptive or harmful response
Dose-dependent effect	Hormetic response	Biphasic dose–response	Benefit or toxicity
Biological outcome	System-level impact	Inflammation and metabolic regulation	Health improvement or impairment
Chronic exposure	Long-term intake	Accumulation and interaction effects	Increased risk of adverse outcomes

4.5. Interpretation of Key Findings

The synthesis demonstrates that natural bioactive compounds exhibit a dual role in food systems, where their effects are determined by a combination of dosage, biological mechanisms, and contextual factors. This duality challenges the common perception that natural compounds are inherently safe and highlights the importance of a more nuanced understanding of their impact. A key insight is that the concept of hormesis provides a valuable framework for explaining the variability in health outcomes associated with natural compounds. This framework emphasizes that both beneficial and harmful effects can arise from the same substance, depending on exposure conditions.

Furthermore, the findings indicate that current approaches to evaluating natural compounds may not fully capture their complexity, particularly in relation to dose-dependent effects and biological interactions. This underscores the need for more integrative and comprehensive frameworks in assessing their safety within food systems.

5. Discussion

The findings emphasize that natural bioactive compounds cannot be evaluated solely based on their beneficial properties, as their effects are inherently dependent on dosage, exposure conditions, and biological context. While these compounds are widely promoted for their therapeutic potential, their widespread use in food systems and supplements increases the likelihood of excessive or unregulated intake. This creates a paradox in which substances recognized for their

health benefits may also pose risks when consumed beyond optimal levels, highlighting the limitations of simplified assumptions regarding the safety of natural products.

Another important implication is the need to reconsider how natural compounds are assessed within food safety frameworks. The concept of hormesis illustrates that biological responses are not linear, and that both beneficial and harmful outcomes can arise from the same compound depending on exposure intensity. In addition, the involvement of mechanisms such as oxidative stress and cellular signaling underscores the complexity of predicting health effects. These findings suggest that current approaches may underestimate the variability and potential risks associated with natural compounds, reinforcing the importance of integrative evaluation methods that account for dose-dependent effects, long-term exposure, and interactions within biological systems.

6. Conclusion

This study demonstrates that natural bioactive compounds in food systems exhibit a dual role, functioning as both beneficial and potentially harmful substances depending on dosage, exposure conditions, and biological context. While these compounds contribute to health promotion through antioxidant, anti-inflammatory, and metabolic effects, their safety cannot be assumed solely based on their natural origin. The findings highlight that the effects of these compounds are dynamic and influenced by multiple interacting factors within food systems and the human body.

From an analytical perspective, the study integrates evidence on functional benefits, hormetic dose–response relationships, toxicity risks, and underlying biological mechanisms. The results indicate that processes such as oxidative stress and cellular signaling play a central role in mediating both protective and adverse effects. This integrated framework emphasizes that natural compounds should be evaluated through a balanced lens that considers both therapeutic potential and toxicological risk.

In practical terms, the findings underscore the need to improve current safety assessment approaches for natural bioactive compounds. Future research should focus on refining dose-response evaluation, understanding long-term exposure effects, and addressing variability in compound composition and usage. Developing more comprehensive and integrative risk assessment frameworks is essential to ensure safe consumption and to support informed use of natural compounds in food systems.

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