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Cytotoxicity of nanosized natural powders

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Abstract

Nanosized natural powders have drawn more attention in pharmaceutical and biological research due to their increased bioavailability, greater cellular absorption, and possible therapeutic efficacy. Traditional medicine frequently uses medicinal plants like clove (*Syzygium aromaticum*), ginger (*Zingiber officinale*), and turmeric (*Curcuma longa*), but their traditional powdered forms frequently have low solubility and limited biological performance. A viable way to get around these restrictions is to nano size these natural particles using physical techniques like ball milling and high-energy grinding. Nanosizing can drastically change physicochemical characteristics and biological interactions despite their natural origin, which raises concerns about safety and cytotoxicity. With an emphasis on *in vitro* cytotoxicity investigations and safety assessment, this article offers a thorough summary of nanosized natural powders. Nanosizing methods, frequently utilizes cell lines and cytotoxicity tests, and underlying mechanisms of cytotoxicity such as oxidative stress, mitochondrial malfunction, apoptosis, and DNA damage. Additionally due considerations were given on safety factors, such dose-dependent toxicity, biocompatibility with normal cells, and regulatory issues. It may be concluded; nanosized ginger, turmeric, and clove powders have shown encouraging therapeutic potential with specific cytotoxicity toward cancer cells; however, additional *in vivo* and clinical research, and systematic safety evaluation are often necessary to ensure their safe pharmaceutical applications.

Keywords: Biological research; Traditional medicine; Oxidative stress; Mitochondrial

1. Introduction

Natural products derived from medicinal herbs have been widely employed in traditional medical systems for ages due to their availability, therapeutic effectiveness, and comparatively low toxicity. Plant-based powders with a variety of pharmacological properties, such as anti-inflammatory, antioxidant, antibacterial, and anticancer actions, including clove, ginger, and turmeric have been in use for addressing various ailments. However, poor water solubility, poor bioavailability, instability, and irregular absorption profiles have limited their clinical use despite their therapeutic potential [1,2]. By reducing particle size to the nanometer range thereby increasing surface area, dissolution rate, and biological contact, the science of nanotechnology has become a viable solution to these constraints in recent years. The

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intricate phytochemical makeup of the parent plant is generally preserved in nanosized natural powders prepared and processed by mechanical techniques; ball milling and high-energy grinding, which have shown enhanced physicochemical and biological characteristics [3,4]. Although it may also change the material's biological behavior and safety profile, nanosizing has demonstrated increased cellular absorption and bioavailability, which may greatly improve therapeutic outcomes [5]. The potential cytotoxicity of nanosized materials is one of the main concern till date. Nanoparticles and nanosized powders can readily interact with cellular membranes, intracellular organelles, and biomolecules due to their smaller size and huge surface area, which can result in oxidative stress, mitochondrial dysfunction, DNA damage, and apoptosis [6]. Unintentional toxicity to normal cells possess serious safety issues, even though such effects might be useful in targeting cancer cells. Therefore, before using nanosized natural powders in pharmacological or biological applications, it is crucial to assess their cytotoxicity [7].

In vitro cell culture models are frequently used in cytotoxicity studies to evaluate cell viability, growth, and death after exposure to nanosized materials. To identify dose-dependent toxicity and specific anticancer potential assays like 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), Lactate dehydrogenase (LDH) release, and apoptosis detection techniques are frequently used [8]. Crucially, a comparison of malignant and normal cell lines has been documented about the biocompatibility and therapeutic selectivity of nanosized natural powders [9]. Due to their rich phytochemical makeup, which includes gingerols, curcuminoids, and eugenol, respectively, ginger (*Zingiber officinale*), turmeric (*Curcuma longa*), and clove (*Syzygium aromaticum*) have drawn a lot of attention among many therapeutic plants. These plant powder's cytotoxic and anticancer properties have been shown to be improved by nanosizing them while preserving acceptable safety limits at lower doses [10–12]. However, the amount of cytotoxicity varied according to particle size, concentration, contact time, and cell line type, highlighting the necessity of a systematic safety assessment.

With an emphasis on ginger, clove, and turmeric, this review attempts to give a thorough summary of the cytotoxicity and safety assessment of nanosized natural powders. Nanosizing techniques, *in vitro* cytotoxicity investigations, cell death processes, and safety evaluation challenges were put forward after a thorough literature review. The logical design and safe use of nanosized natural powders in the pharmaceutical and biomedical industries depend on an understanding of these challenges.

2. Nanosized Natural Powders: An Overview

Plant-based materials that have been mechanically or physically reduced to the nanometer-sized while maintaining their inherent phytochemical makeup were referred to as nanosized natural powders. Nanosized natural powders are usually made via size-reduction using a ball mill and high-energy grinder, which maintains the holistic nature of the plant material, in contrast to nanoparticle systems created by chemical or biological techniques. Because of its ease of use, affordability, and compatibility with treatments based on natural products, this method has drawn more and more interest in pharmaceutical and biomedical research [4,13].

2.1. Concept and Characteristics of Nanosized Natural Powders

Powdered plant materials with particle sizes usually less than 1000 nm, frequently between 50 and 500 nm, are referred to as nanosized natural powders. Surface area is greatly increased by reduction to the nanoscale, improving wettability, dissolving rate, and contact with biological membranes. When compared to their bulk equivalents, these powders frequently have shown better physicochemical characteristics, such as improved solubility, homogeneous particle distribution, and greater bioactivity [14,15]. Safety assessment is a crucial part of their development, though, since the shrinkage may potentially change surface reactivity.

2.2. Methods of Nanosizing Natural Powders

Nanosized natural powders are prepared using a variety of physical ways, the most popular being mechanical procedures. The various processing methods are summarized in subsequent texts.

2.2.1. Ball Mill

Ball milling is a popular mechanical size-reduction method that uses grinding media to repeatedly contact and friction plant particles. While preserving chemical stability, high-energy ball milling can efficiently reduce particle size to the nanometer region. Because it doesn't need excessive temperature or chemical reagents, this approach is especially appropriate for natural compounds that are sensitive to heat [16].

2.2.2. High-Energy Mill

Intense mechanical forces are used in high-energy milling to reduce plant materials to nanoscale particles. This technique offers more control over particle size distribution and consistency than traditional milling. It has been effectively used to increase the biological activity of herbal powders like clove, ginger, and turmeric [13,17].

2.2.3. Mechanical Grinder and Pulverization

To produce nanoscale particle sizes, mechanical grinding and pulverization processes use shear forces and repeated crushing. To produce consistent nanosized particles, this technique is frequently used in conjunction with screening or secondary milling, despite being less energy-intensive than ball milling [18].

2.3. Advantages of Nanosizing Natural Powders

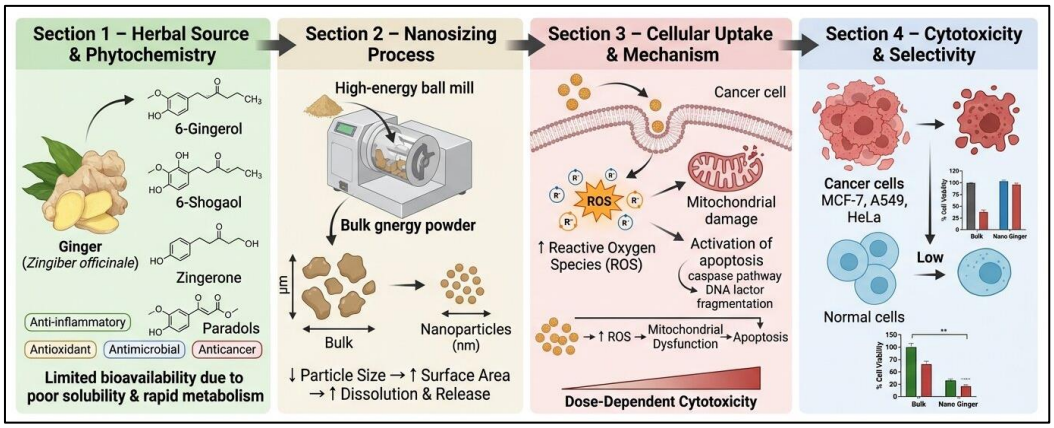
There are various pharmacological benefits of nanosizing natural powders; due to the improved solubility and absorption caused by the larger surface area, phytoconstituents are more bioavailable. Nanosized herbal powders have been demonstrated to have improved cellular absorption, which leads to increased therapeutic efficacy, especially in antioxidant and anticancer applications [19]. Furthermore, nanosized powders may minimize side effects by enabling dose reduction without compromising therapeutic efficacy. Despite these benefits, cellular biological interactions can be impacted by nanosizing. Cytotoxic effects could result from increased reactivity and improved cellular penetration, particularly at higher doses. Therefore, to assure the safe use of nanosized natural powders in pharmaceutical formulations, thorough cytotoxicity and safety assessments are essential [7].

3. Selected Natural Products Used for Cytotoxicity Studies:

Herbal remedies were thought to be among the bioactive substances that may provide a variety of biological effects. Due to their diverse pharmacological characteristics and effective nanosizing, ginger, turmeric, and clove have been increasingly popular in recent years. Following nanosizing, powdered versions of these herbal remedies exhibit improved biological activity and cellular affinity, making them suitable for cytotoxicity investigations.

3.1. Ginger (*Zingiber officinale*)

Due to its anti-inflammatory, antioxidant, antibacterial, and anticancer properties, ginger has long been used as a medicinal herb. Numerous bioactive substances, including as paradols, zingerone, 6-gingerol, and 6-shogaol, are found in its rhizome. Unfortunately, due to its rapid metabolism and poor water solubility, ginger in its usual powdered form has poor bioavailability.



Source: Authors own illustration

Figure 1 Improving the anticancer potential of ginger through nanosizing.

Ginger powder's physicochemical properties and biological performance have been demonstrated to be enhanced by nanosizing it using high-energy ball milling. Reducing the particle size greatly increases the surface area, which facilitated a greater release of the active phytochemicals. Consequently, this improved overall efficacy and cellular uptake. Nanosized ginger powder has been shown *in vitro* to exhibit cytotoxic effects on many cancer cell lines, such as Michigan cancer foundation-7 (MCF-7), human alveolar basal epithelial cells (A549), and Henrietta Lacks cells (HeLa), in a dose-dependent way **(Figure 1)**. These effects were mostly linked to the development of oxidative stress, which

causes cancer cells to undergo apoptosis. Simultaneously, it has been noted that the nanosized form exhibits much lower toxicity against normal cell lines at defined dosages, indicating a level of selective cytotoxic action [10,20,21].

3.2. Turmeric (*Curcuma longa*)

The presence of curcuminoids, such as curcumin, demethoxycurcumin, and bisdemethoxycurcumin, makes turmeric one of the most researched therapeutic plants. The antioxidant, anti-inflammatory, antibacterial, and anticancer qualities of curcumin are widely recognized. Turmeric's weak bioavailability, low stability, and poor water solubility limit its clinical use despite its medicinal value.

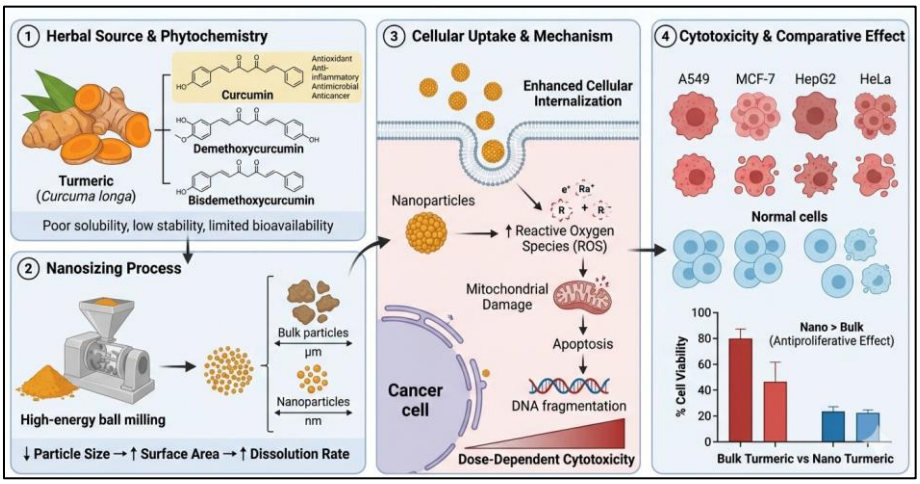


Figure 2 Improved anticancer potential of nanosized turmeric particles. Source: Authors own illustration

Ball milling resulted in nanosized turmeric powder, which Increased the rate of curcuminoid dissolution and cellular internalization while mechanical nanosizing improved biological activity. Nanosized turmeric powder has been shown to have strong antiproliferative effects against cancer cell lines like A549, MCF-7, Human liver cancer cell line (HepG2), and HeLa in a number of *in vitro* cytotoxicity experiments **(Figure 2)**. The primary causes of the harmful effects included mitochondrial dysfunction, increased production of reactive oxygen species, and apoptosis induction. According to comparative studies, nanosized turmeric powder have demonstrated suitable safety profiles in normal cell lines and is more efficient than bulk turmeric powder [11,22,23].

3.3. Clove (*Syzygium aromaticum*)

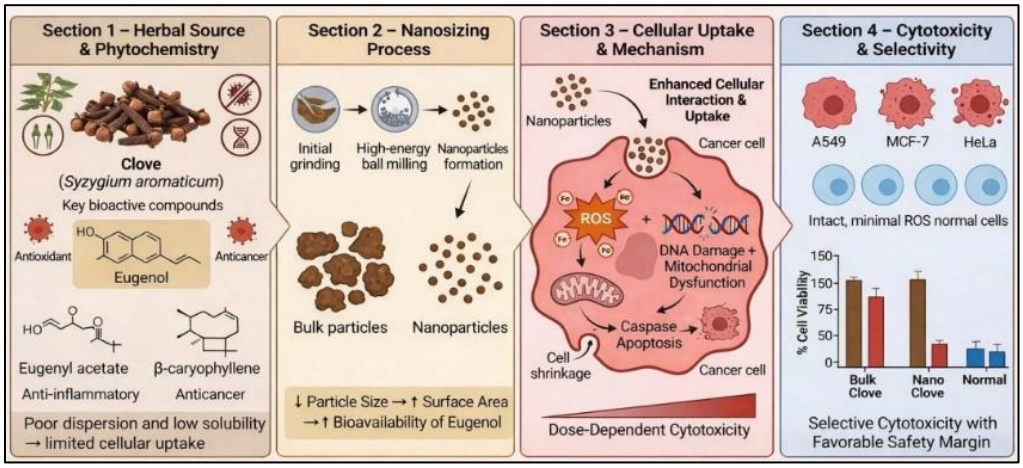


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Figure 3 Effect of particle size reduction on the cytotoxic potential of clove.

Eugenol, eugenyl acetate, and β-caryophyllene are among the bioactive chemicals found in clove, a fragrant spice and medicinal plant. These substances have shown strong antibacterial, anti-inflammatory, anticancer, and antioxidant properties. However, because of its poor dispersion and solubility, conventional clove powder has minimal cellular absorption.

Clove powder's cytotoxic potential was increased by nanosizing it using ball milling after initial grinding, which increased eugenol's bioavailability and contact with cellular membranes **(Figure 3)**. Studies on *in vitro* cytotoxicity have shown that nanosized clove powder causes oxidative stress, DNA damage, and death in cancer cell lines such as A549, MCF-7, and HeLa. Nanosized clove powder has been shown to be minimally toxicity to normal cell lines at lower doses, indicating a favorable safety margin when dosed adequately [24–26].

3.4. Rationale for Selecting Ginger, Turmeric, and Clove

The selection of ginger, turmeric, and clove for cytotoxicity studies was based on their rich phytochemical content, proven therapeutic value, and appropriateness for physical nanosizing. In their traditional forms, these plants are commonly ingested natural products with established safety profiles. Their biological activity was increased by nanosizing, however thorough cytotoxicity and safety assessment are required. As a result, these natural products are perfect examples for comprehending the safety concerns and cytotoxic behavior of nanosized natural powders.

4. *In vitro* Cytotoxicity Studies of Nanosized Natural Powders

In vitro cytotoxicity studies are essential for assessing the biological safety and therapeutic effectiveness of nanosized natural powders. In order to evaluate cell survival, proliferation, membrane integrity, and apoptosis after exposure to nanosized materials, these investigations are usually carried out using cultivated cancer and normal cell lines. Prior to *in vivo* studies, the results offer first hand understanding of dose-dependent toxicity, selective anticancer activity, and possible safety issues. Due to their larger surface area and better cellular absorption, nanosized natural powders show greater cellular contact. The need for systematic evaluation utilizing standardized *in vitro* assays is highlighted by the possibility that cytotoxic effects could be increased when compared to traditional bulk powders [19,27].

4.1. Cell Lines Used for Cytotoxicity Evaluation

Nanosized natural powders are tested for selective cytotoxicity and biocompatibility using both malignant and normal cell lines as depicted in **Table 1.**

Table 1 Common Cell Lines Used in *In vitro* Cytotoxicity Studies

Cell line	Cell type	Purpose
MCF-7	Human breast cancer	Anticancer activity
A549	Human lung carcinoma	Antiproliferative evaluation
HeLa	Human cervical cancer	Cytotoxicity screening
HepG2	Human liver cancer	Metabolic toxicity
HT-29	Human colon cancer	Anticancer potential
L929	Mouse fibroblast (normal)	Biocompatibility
Vero	Normal kidney epithelial	Safety evaluation

4.2. Cytotoxicity Assays Commonly Employed

The cytotoxic effects of nanosized natural powders are generally evaluated using a variety of biochemical and microscopy tests as summarized in Table 2.

Table 2 Common *In vitro* Cytotoxicity Assays

Assay	Principle	Endpoint
MTT assay	Reduction of MTT by mitochondrial enzymes	Cell viability
XTT / WST-1	Metabolic activity measurement	Cell proliferation
LDH assay	Release of LDH due to membrane damage	Cytotoxicity
Trypan blue exclusion	Dye uptake by dead cells	Cell viability
Annexin V/PI staining	Phosphatidylserine exposure	Apoptosis
Comet assay	DNA strand breaks	Genotoxicity

4.3. Cytotoxicity Profile of Nanosized Ginger Powder

Nanosized ginger powder has been shown *in vitro* to have strong dose-dependent cytotoxic effects on a variety of cancer cell lines as cited in **Table 3.** Increased oxidative stress, mitochondrial malfunction, and apoptotic cell death are caused by increased gingerol and shogaol production. At same doses, normal cell lines typically show reduced sensitivity.

Table 3 *In vitro* Cytotoxicity Studies of Nanosized Ginger Powder

Cell line	Assay	Concentration range	Key findings	Reference
MCF-7	MTT	25–150 µg/mL	IC_{50} ~80 µg/mL; apoptosis induction	[28]
A549	MTT	50–200 µg/mL	ROS-mediated cytotoxicity	[29]
HeLa	LDH	25–100 µg/mL	Membrane damage & apoptosis	[30]
L929	MTT	≤50 µg/mL	Minimal toxicity	[31]

4.4. Cytotoxicity Profile of Nanosized Turmeric Powder

Nanosized turmeric powder exhibits higher cytotoxic effect than bulk turmeric because curcuminoids are better absorbed by cells. Studies have shown that at lower dosages, there are notable antiproliferative effects in cancer cells while retaining acceptable safety profiles in normal cells. The findings are summarized in **Table 4.**

Table 4 *In vitro* Cytotoxicity Studies of Nanosized Turmeric Powder

Cell line	Assay	Concentration range	Key findings	Reference
A549	MTT	10–100 µg/mL	Cell cycle arrest & apoptosis	[12]
MCF-7	MTT	20–120 µg/mL	ROS generation; caspase activation	[32]
HepG2	LDH	25–150 µg/mL	Dose-dependent cytotoxicity	[33]
L929	MTT	≤75 µg/mL	Biocompatible	[22]

4.5. Cytotoxicity Profile of Nanosized Clove Powder

Strong cytotoxic activity in nanosized clove powder was linked to increased eugenol bioavailability. Studies conducted *in vitro* have shown that cancer cells are induced to undergo oxidative stress, DNA damage, and death, with minimal harm to normal cells at regulated dosages as depicted in **Table 5.**

Table 5 *In vitro* Cytotoxicity Studies of Nanosized Clove Powder

Cell line	Assay	Concentration range	Key findings	Reference
A549	MTT	20–100 µg/mL	DNA fragmentation; apoptosis	[34]
MCF-7	Annexin V/PI	25–80 µg/mL	Early & late apoptosis	[26]
HeLa	LDH	30–120 µg/mL	Membrane disruption	[25]
Vero	MTT	≤50 µg/mL	Low cytotoxicity	[35]

4.6. Summary of *In vitro* Findings

When compared to their bulk equivalents, nanosized ginger, turmeric, and clove powders often exhibited more cytotoxic effects against cancer cell lines. Normal cells showed comparatively reduced sensitivity, confirming their potential therapeutic selectivity, whereas the observed cytotoxicity was mostly dose-dependent and mediated by oxidative stress and death. However, differences in test techniques, particle size, and experimental settings emphasized the significance of standardized evaluation procedures.

5. Mechanisms of Cytotoxicity of Nanosized Natural Powders

The primary cause of the harmful effects of nanosized natural powders might be due to their increased surface area and decreased particle size, which might result in improved interaction with cellular components **(Figure 4)**. Bioactive phytoconstituents are better absorbed by cells due to nanosizing, which increases biological reactions. Oxidative stress induction, mitochondrial malfunction, apoptosis, DNA damage, and cell cycle arrest are the main processes underlying the cytotoxic impact of nanosized natural powders including ginger, turmeric, and clove [36].

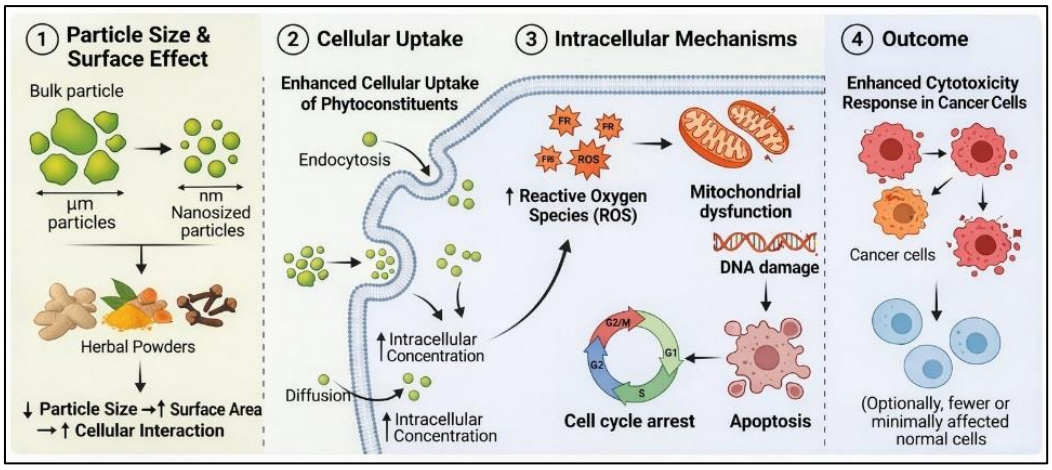

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Figure 4 Mechanistic overview of cytotoxic effects induced by nanosized natural powders

5.1. Cellular Uptake and Intracellular Interaction

Natural powders at the nanoscale are easily absorbed by cells through passive diffusion and endocytosis. Once inside the cell, these particles produce bioactive substances near intracellular targets, including eugenol, curcuminoids, and gingerols. This increased intracellular availability triggers cytotoxic signalling pathways by increasing contact with nuclear material, lysosomes, and mitochondria [5].

5.2. Reactive Oxygen Species (ROS) Generation

The overproduction of reactive oxygen species is one of the main ways whereby nanosized natural powders cause cytotoxicity. Oxidative stress is caused by elevated ROS levels upsetting the cellular redox equilibrium. Cellular lipids, proteins, and DNA can be harmed by excessive ROS, which eventually results in cell death. Cancer cells are especially sensitive to further oxidative damage from nanosized phytoconstituents since they already have high basal ROS levels [37,38].

5.3. Mitochondrial Dysfunction

ATP production is hampered and the mitochondrial membrane depolarises as a result of ROS-mediated oxidative stress. Pro-apoptotic elements like cytochrome c are released into the cytoplasm when mitochondrial integrity is compromised. The intrinsic apoptotic pathway, which is marked by the activation of caspase-9 and then caspase-3, is triggered by this event [39].

5.4. Induction of Apoptosis

One important mechanism that underlies the cytotoxic impact of natural powders in nanoscale form is apoptosis. Pro-apoptotic proteins (Bax) are upregulated and anti-apoptotic proteins (Bcl-2) are downregulated when apoptotic signalling pathways are activated. DNA fragmentation, chromatin condensation, and programmed cell death result from the executioner caspases' subsequent activation. At lower doses, nanosized ginger, turmeric, and clove powders have been shown to preferentially cause apoptosis in cancer cells while sparing normal cells [40,41].

5.5. DNA Damage and Cell Cycle Arrest

DNA strand breakage and chromosomal damage can result from excessive ROS and direct contact of nanoparticles with nuclear material. Cell cycle checkpoints are triggered by this genotoxic stress, resulting in arrest at the G0/G1 or G2/M phases. Cell cycle arrest contributes to the overall cytotoxic effect by inhibiting the growth of injured cells and promoting apoptotic elimination [42].

5.6. Schematic Representation of Cytotoxic Mechanisms

Table 6 Schematic Overview of Cytotoxic Mechanisms of Nanosized Natural Powders

Step	Mechanism	Cellular Effect	Outcome
1	Cellular uptake of nanosized powders	Enhanced intracellular phytoconstituent release	Increased bioavailability
2	ROS generation	Oxidative stress	Cellular damage
3	Mitochondrial dysfunction	Loss of membrane potential, ATP depletion	Apoptotic signalling
4	Caspase activation	Caspase-9 and caspase-3 activation	Apoptosis
5	DNA damage	Strand breaks and chromosomal instability	Cell cycle arrest
6	Cell cycle arrest	G0/G1 or G2/M phase arrest	Inhibition of proliferation
7	Programmed cell death	Apoptosis	Elimination of cancer cells

5.7. Overall Mechanistic Insight

A multi-targeted mechanism including oxidative stress, mitochondrial damage, and apoptotic pathways mediates the lethality of nanosized natural powders. These mechanisms work in concert to increase anticancer activity while allowing selective toxicity to cancerous cells. However, normal cells may also be impacted by high concentrations or excessive exposure, underscoring the significance of dose optimisation and safety assessment.

6. Safety Evaluation of Nanosized Natural Powders

When developing nanosized natural powders for use in pharmaceutical and biological applications, safety evaluation is a crucial stage. Nanosizing can dramatically change the biological behaviour, cellular interactions, and toxicity profile of natural compounds, even though they are widely regarded as safe in their traditional forms. In order to ensure its safe use, comprehensive safety assessment is crucial.

6.1. Importance of Safety Evaluation at the Nanoscale

Natural powders at the nanoscale have special physicochemical characteristics such smaller particles, more surface area, and improved surface reactivity. These characteristics promote therapeutic efficacy and bioavailability, but they may also raise the risk of adverse cellular interactions. Nanosized powders can interact with intracellular organelles,

cross cellular membranes, and cause unintentional toxic reactions because of small size. Therefore, prior to clinical or pharmacological application, a comprehensive safety evaluation is required [7].

6.2. *In vitro* Cytotoxicity Assessment Using Normal Cell Lines

The first stage of safety review must be, *in vitro* cytotoxicity testing, which is often carried out using normal cell lines such Vero cells and mouse fibroblast cell line (L929). These studies aid in determining whether natural powders at the nanoscale have harmful impacts on healthy cells. Therapeutic selectivity can be understood by comparing the cytotoxicity of malignant and normal cells. When nanosized natural powders exhibit selective toxicity toward cancer cells while exhibiting low toxicity toward normal cells at therapeutic dosages, they are typically regarded as safer [43].

6.3. Dose-Dependent Toxicity Evaluation

Natural powders at nanoscale have a very dose-dependent toxicity. Higher quantities of these substances can cause oxidative stress, membrane damage, and cell death, whereas lower doses may be biocompatible and therapeutically advantageous. Therefore, it is crucial to use dose-response experiments to determine the safe concentration range. Safe exposure limits can be defined by establishing IC_{50} values and no-observed-adverse-effect levels (NOAEL) [5].

6.4. Comparison Between Bulk and Nanosized Natural Powders

Comparing nanosized particles to their bulk equivalents is another aspect of safety evaluation. Due to better cellular absorption, nanosized natural powders have been shown in multiple studies to have higher biological activity than bulk powders. But this increased activity might also make it more cytotoxic. To determine if nanosizing creates new safety risks or only intensifies pre-existing biological effects, comparative research is essential [5,44].

6.5. Oxidative Stress-Mediated Toxicity

One important mechanism behind the toxicity caused by nanomaterials is oxidative stress. Excessive reactive oxygen species (ROS) produced by nanosized natural powders can cause DNA damage, lipid peroxidation, and protein oxidation. While excessive ROS can damage healthy cells and tissues, moderate ROS formation may have anticancer benefits. As a result, assessing oxidative stress markers is a crucial part of safety evaluation [5,37].

6.6. Role of *In Vitro* Assays in Safety Evaluation

Cell viability, membrane integrity, and mode of cell death are frequently evaluated using common *in vitro* tests like MTT, LDH release, and apoptosis assays. These tests offer quick and affordable cytotoxic potential screening. The necessity for standardised testing procedures is highlighted by the fact that results can differ according on cell type, assay settings, and exposure period [45].

6.7. Biocompatibility of Nanosized Herbal Powders

According to a number of studies, when utilised within specific dosage ranges, nanosized herbal powders have shown adequate biocompatibility. When correctly manufactured and dosed, nanosized natural compounds can be safely used, according to safety evaluation utilising both in-vitro and in-vivo models. However, chronic toxicity and long-term exposure data are still scarce, highlighting the need for more research [13].

6.8. Regulatory and Translational Considerations

Before being approved for use in pharmaceuticals, nanosized natural powders must pass rigorous safety testing [5]. Standardised toxicity testing, nanomaterial characterisation, and in-vivo validation of in-vitro results are all stressed by regulatory bodies [46]. For nanosized natural powders to successfully transition from laboratory research to clinical use, these issues must be resolved [47].

7. Conclusion

By increasing bioavailability and cellular contact, nanosized natural powders offer a viable way to boost the therapeutic potential of medicinal plants, through processes like oxidative stress, mitochondrial malfunction, and apoptosis. Nanosizing powders of ginger, turmeric, and clove has shown increased *in vitro* cytotoxic action, especially against cancer cell types. Crucially, at controlled concentrations, these nanosized powders typically show reduced toxicity toward normal cells, suggesting selective cytotoxic potential. Nanosizing may, however, potentially change safety profiles, highlighting the necessity of thorough dose-dependent toxicity assessment. All things considered, nanosized natural powders have a lot of promise for use in pharmaceutical and biomedical applications. However, to guarantee

their safe and efficient usage, systematic safety evaluation, standardised manufacturing techniques, and additional in-vivo and clinical research are crucial.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Author Contribution

First author: Concept. Second author: Data accumulation. Third author: Design and drafting. Fourth author: Data validation. Corresponding author: Overall validation

Data Availability

Data is available from the corresponding author on request.

Statement of Usage of Artificial Intelligence

Open AI platforms were used for grammatical corrections only.

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