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Review

# The Significance of Truffles for Human Health

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**ABSTRACT:** Truffles are hypogeous fungi predominantly of the phylum Ascomycota that have been historically valued for their dual significance as culinary delicacies and therapeutic agents. Indigenous communities in the Middle East and North Africa (MENA) traditionally used desert truffles as aphrodisiacs and to treat ocular and inflammatory conditions. At the same time, European sources have documented the medicinal and nutritional significance of the truffles since the 17th century. Truffles are rich in functional compounds, including terpenoids, polysaccharides, phenolic compounds, and essential fatty acids. Several studies suggest that these bioactive compounds exhibit antioxidant, antimicrobial, anti-inflammatory, anticancer, and immunomodulatory properties. The nutritional value of truffles has proteins/amino acids, dietary fibers, vitamins, and minerals. Recently, silver nanoparticles synthesized from desert truffles showed antibacterial and antifungal activities. These nutritional attributes may help prevent lifestyle-related diseases such as diabetes, cardiovascular disorders, and cancer. This review introduces the ethnomedicinal, nutritional, biochemical, and pharmacological evidence on truffles, emphasizing their possible integration into functional foods and therapeutic strategies.

**Keywords:** Truffle, Sustainable Nutrition, Ethnomedicine, Bioactive Compounds, Natural Therapeutics, Functional Foods.

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## 1. INTRODUCTION

The truffle is a hypogeous macrofungus mainly belonging to the phylum Ascomycota, defined by underground fruiting bodies and strong ecological interactions with host plants. Some species in the genera *Tuber*, *Terfezia*, and *Tirmania* form ectomycorrhizal associations, enabling nutrient exchange, enhancing soil fertility, and improving plant resilience, particularly in arid and semi-arid ecosystems (El Enshasy et al., 2013; Hilszczańska et al., 2014). The last ecological features, combined with their distinctive aroma and flavor, position truffles at the interface of environmental biology, gastronomy, and human health (Owaid, 2016).

However, truffles have been central to traditional food systems and medical practices across the Middle East and North Africa (MENA). Desert truffles were harvested seasonally, consumed as nutrient-rich foods, and used as therapeutic resources. Ethnomedicinal records and oral traditions report their use for ocular disorders, inflammatory conditions, and reproductive health, including applications as aphrodisiacs (Owaid, 2018; Mandeel & Al-Laith, 2007; Tayjanov et al., 2021). However, the value of truffles is incorporated into culinary and medicinal traditions as recorded in European history (Hilszczańska et al., 2017).

Several studies have broadened our understanding of truffles beyond their flavor and aroma, showing a diverse nutritional and biochemical profile. They are rich in essential amino acids (proteins), dietary fibers, vitamins, and minerals, while maintaining relatively low lipid content (Üstün et al., 2018; Lee et al., 2020; Khan et al., 2022). Truffles also contain a broad range of bioactive molecules, including polysaccharides, terpenoids, phenolic compounds, and volatile organic compounds, which contribute to their reported biological functions (Villares et al., 2012; Mustafa et al., 2020).

*In vitro* studies increasingly indicate the therapeutic potential of truffles, showing antioxidant, antimicrobial, anti-inflammatory, anticancer, and immune-enhancing effects in both in vitro and in vivo models (Janakat et al., 2004a; Beara et al., 2014; Al Obaydi et al., 2020). Despite promising laboratory findings, translating these effects into clinical practice remains limited due to a lack of human trials and variability across truffle species (Baldelli et al., 2025).

Even now, most studies examine European forest truffles, with no research on the local medicinal uses of desert truffles (El Enshasy et al., 2013). In addition, although edible mushrooms have been studied in functional foods and nutraceuticals, truffles have received comparatively less attention in applied nutritional and biomedical research.

This review examines the integration of ethnomedicinal knowledge, its nutritional and pharmacological benefits, and the significance of truffles for human health. This work emphasizes the potential of truffles as functional foods and sources of biologically active compounds, while highlighting critical areas that require further investigation and clinical validation.

## 2. ETHNOMEDICAL AND CULINARY SIGNIFICANCE

Historically, truffles were highly appreciated across different cultures and places for their health benefits and culinary value, which can be found in North African, Middle Eastern and European culture. Desert truffles, including *Terfezia claveryi*, have been employed for ages by African communities as aphrodisiacs and in the treatment of ocular disease (Mandeel & Al-Laith, 2007; El Enshasy et al., 2013). In addition, *Tirmania nivea* is consumed as a nutrient and anti-inflammatory agent in the Middle East and North Africa (MENA\) (Al-Laith, 2010; Tayjanov et al., 2021).

The Tuber aestivum has been reported to be used for culinary and antioxidantes properties (Rosa-Gruszecka et al., 2017). Desert truffles have been used as aphrodisiacs among African and Middle Eastern communities and are also recognized to exhibit an anti-inflammatory effect. In Europe, ancient uses have been derived to options for alimentary purposes; the product is presented in this paper as a chatbot since consumption and disease prevention depend on regional differences (Baldelli et al., 2025). It has been demonstrated that *Terfezia boudieri*, a Middle Eastern species, produced the immunomodulatory and anticancer functions in various researches (Al Obaydi et al., 2020). These ethnomedicinal uses, recorded by oral tradition and historical sources, indicate the sustained cultural relevance of truffles, and serve as a basis for contemporary perspectives on their health-beneficial effects, as discussed in Table 1.

**Table 1**. Ethnomedicinal uses of Truffles.

| Truffle Species | Region | Traditional Use | Reference |
|---|---|---|---|
| *Terfezia claveryi* | Africa, Middle East | Aphrodisiac, ocular treatments | El Enshasy et al., 2013; Mandeel & Al-Laith, 2007 |
| *Tirmania nivea* | North Africa, Middle East | Nutritional supplement, anti-inflammatory | Al-Laith, 2010; Tayjanov et al., 2021 |
| *Tuber aestivum* | Europe (Poland) | Culinary, antioxidant | Al Obaydi et al., 2020; Rosa-Gruszecka et al., 2017 |
| *Terfezia boudieri* | Middle East | Immunomodulatory, anticancer | Hilszczańska et al., 2014 |

## 3. NUTRITIONAL COMPOSITION

In comparison, truffles presented a balanced macronutrients and micronutrients profile. They are characterized by high level of proteins, essential amino acids, and dietary fibers with a low fat content (Üstün et al., 2018). In addition, truffles are also a good source of minerals like potassium, calcium, magnesium, and phosphorus (see Table 2). The parts are compatible with human metabolism and physical activities.

The chemical composition of truffles is highly variable and depends on species, ecological conditions, development stage as well as soil characteristics (Rondolini et al, 2024). The carbohydrate and fiber content are higher in desert truffles, compared with forest ones (Lee et al., 2020), but the fruiting bodies of forest truffles can have more lipid and volatile compounds. This diversity underscores the necessity to perform species-specific studies in order to evaluate the nutritional and functional properties of truffles.

**Table 2**. Nutritional Composition and Energy Content of Selected Truffle Species.

| Species | Protein (%) | Fat (%) | Carbohydrate (%) | Fiber (%) | Minerals (mg/100 g) | Energy (kcal/100 g) | References |
|---|---|---|---|---|---|---|---|
| *Terfezia claveryi* | 15.4 | 1.8 | 60.2 | 12.3 | Fe: 6.5, Zn: 3.2 | 338 | Üstün et al., 2018 |
| *Tirmania nivea* | 12.8 | 2.1 | 65.0 | 10.5 | Fe: 5.8, Zn: 2.9 | 34-65 (Fresh wt) | Al-Laith, 2010 |
| *Tuber aestivum* | 14.2 | 3.5 | 55.0 | 9.8 | Fe: 7.2, Zn: 3.5 | 411 | Al Obaydi et al., 2020; Villares et al., 2012 |
| *Terfezia boudieri* | 16.0 | 2.0 | 58.7 | 11.2 | Fe: 6.0, Zn: 3.0 | Not reported | |
| *Terfezia arenaria* | 14.8 | 1.9 | 62.0 | 11.5 | K: 3695, P: 1407, Mg: 128, Ca: 95, Fe: 6.1, Zn: 3.2, Cu: 0.4, Mn: 0.3, Se: 0.02 | 324 | Ferreira et al., 2023 |

* **Legend**: Energy values are reported as dry weight unless otherwise specified. Fresh weight values are not directly comparable.

## 4. BIOACTIVE COMPOUNDS IN TRUFFLES

The health properties of truffles are primarily related to their various bioactive compounds. Some of these molecules can be polysaccharides, terpenoids, phenolic compounds, sterols, and volatile organic compounds (VOCs) (Al Obaydi et al., 2020; El Enshasy et al., 2013; Lee et al., 2020). Some isolated immune-modifying polysaccharides, especially β-glucans, are widely studied for their immunomodulatory, anti-tumor, and prebiotic properties. In vitro experiments demonstrated that β-glucans obtained from truffles were able to promote macrophage activity, increase lymphocyte proliferation, and modulate cytokine production. This concept provides a mechanistic understanding of putative functions in immune support and cancer prevention (Li et al., 2018; Tejedor-Calvo et al., 2020).

Additionally, phenolic compounds (phenolic acids and flavonoids) are major contributors to the antioxidant potential of truffles. These molecules scavenge the deleterious free radicals and quench reactive oxygen species (ROS). They then diminish oxidative stress associated with chronic diseases like diabetes, cardiovascular illnesses and cancer (Villares et al., 2012; Friedman, 2016).

On the other hand, terpenoids and sterols also enhance the bioactivity of truffles. The bioactivity includes demonstrating anti-inflammatory, antimicrobial, and hepatoprotective effects (Lee et al., 2020). Volatile organic compounds (VOCs) give truffles their distinctive smell, and they include sulfur compounds, ketones, alcohols, and aromatic hydrocarbons. Beyond aroma, some VOCs may have antimicrobial and signaling roles (Table 3), which could affect both ecological interactions and possible effects on the body (Strojnik et al., 2020).

In general, the amount and type of these active compounds vary between truffle species. They can also vary with truffle growth stage, environmental conditions, and extraction method, so standardized analysis is needed to evaluate their nutritional and medicinal benefits reliably (Lee et al., 2020).

**Table 3**. Selected Truffle Species and Bioactive Compounds

| Truffle Species | Major Bioactives | Observed Activities | References |
|---|---|---|---|
| *Terfezia boudieri* | Polysaccharides<br>Terpenoids | Immunomodulatory, & anticancer (preclinical) | (Al Obaydi et al., 2020; El Enshasy et al., 2013; Lee et al., 2020) |
| *Tuber aestivum* | Phenolics<br>Ergosteryl esters | Antioxidant, & antimicrobial | (Al-Laith, 2010; Villares et al., 2012; Beara et al., 2014) |
| *Tirmania nivea* | Polysaccharides<br>Terpenoids | Immunostimulatory & cytotoxic (*in vitro*) | (Pattanayak et al., 2017; Dyary et al., 2020; Taş et al., 2021) |

## 5. BIOACTIVITIES OF TRUFFLES

Truffles contain a range of functional constituents. These compounds have been linked to several therapeutic properties, including antioxidant, antimicrobial, anticancer, and immunomodulatory effects. Several studies (Villares et al., 2012; Al Obaydi et al., 2020; Lee et al., 2020) reported consistent findings.

### 5.1. Antioxidant Activity

The genera *Tuber*, *Terfezia*, and *Tirmania* are the most commonly eaten truffle genera. These truffles are categorized into two larger types: forest truffles, which are classified by the *Tuber* genus, and desert truffles (arid, semi-arid zones), which are part of the *Terfezia*, *Tirmania*, and *Picoa* varieties. *In vitro* studies show that truffles have a high concentration of antioxidant compounds, which can neutralize free radicals as measured by assays such as DPPH, and reduce biologically relevant ROS, including hydroxyl radical, under laboratory conditions (Guo et al., 2011; Beara et al., 2014; Ferlay et al., 2015; Patel et al., 2017). A class of naturally occurring chemicals called antioxidants can help reduce oxidative stress in the body. Because the body uses oxygen regularly, free radicals are continuously produced. These free radicals cause cell damage in the body and are linked to several illnesses, including cancer, diabetes, and heart disease. As demonstrated in preclinical studies, antioxidants can scavenge free radicals and reduce cellular oxidative stress (Mamta et al., 2014).

Antioxidants (a variety of substances found in foods, in the body, or both) can slow, regulate, or halt oxidative events (which can lead to deterioration of food quality or the appearance and spread of degenerative diseases throughout the body) when present in small quantities in a biological system. Counteracting oxidative processes through these antioxidant molecules involves multiple mechanisms (Shahidi and Zhong, 2015). The body produces endogenous antioxidants such as glutathione, while additional antioxidants are obtained from diet or supplements. There are two categories of antioxidants: primary and secondary antioxidants. Antioxidants function as hydrogen donors or acceptors of free radicals, preventing the propagation of the oxidation chain reaction and producing more stable radicals instead (Munteanu and Apetrei, 2021). Generally, polysaccharides, terpenoids, and phenolics, which are classified as antioxidant compounds, also exhibit anti-inflammatory characteristics (Elsayed et al., 2014; Friedman, 2016). Oxidative stress is associated with inflammatory disorders, particularly in the case of diabetes mellitus (DM). This relationship results from hyperglycemia, a typical indicator of DM, which leads to an overproduction of free radicals (Muriach et al., 2014).

However, truffles contain secondary antioxidant metabolites, such as tocopherols, flavonoids, phytosterols, and carotenoids. Phenolics, which act as scavengers of free radicals, can be highly effective antioxidants due to their ability to donate hydrogen or electrons as reducing agents (Rice-Evans et al., 1997). The antioxidant power of *T. aestivum* was found to be closely associated with its highest levels of phenolics and ergosteryl esters among the three species (Villares et al., 2012). Additionally, the diverse secondary metabolites of desert truffle species also encompass various antioxidant compounds. *T. nivea* exhibited a significantly greater total phenolic content compared to the species *T. pinoyi* and displayed a higher antioxidant activity as well (Hamza et al., 2016; Al-Laith, 2010).

### 5.2. Antimicrobial Activity

Antimicrobial activity of truffles was studied. Generally, truffles have shown antimicrobial activity, acting against both Gram-positive and Gram-negative bacteria. *In vitro* studies indicate that aqueous extracts of *Terfezia claveryi* can inhibit the growth of *Staphylococcus aureus*, a common pathogen associated with skin and systemic infection (Janakat et al., 2004a). Beyond traditional aqueous extracts, nanotechnology-based approaches have enhanced truffle antimicrobial properties. For example, silver nanoparticles synthesized from *Tirmania* species exhibit broad-spectrum antibacterial effects, effectively targeting both Gram-negative and Gram-positive bacteria, including strains resistant to conventional antibiotics (Owaid et al., 2018; Owaid, 2022). In addition, silver nanoparticles synthesized from *Picoa* showed antifungal activities (Owaid et al., 2022).

Generally, truffle-derived compounds have also shown activity against other pathogenic microorganisms, including *Escherichia coli* and *Staphylococcus epidermidis*. Casarica et al. (2016b) referred that the aqueous extract of *T. claveryi* could inhibit these pathogens, suggesting potential applications in ocular infections and possibly other localized microbial infections. Preclinical in vitro studies indicate that certain truffle extracts can inhibit microbial growth under laboratory conditions through mechanisms that may involve disruption of cell membranes, interference with microbial metabolic pathways, or modulation of microbial oxidative stress (Taş et al., 2021). In addition, the extracts of *T. claveryi* showed antibacterial activity against *Streptococcus pneumoniae* (*in vivo*) (Radif et al., 2019).

Several studies have reported that truffle-enriched compounds might, in vitro, exert effects which are consistent with traditional uses ascribed to them in African and Middle Eastern countries of origin (for whom they served as cures for infections and injuries) (El Enshasy et al., 2013). The bioactivity can be attributed, at least in part, to the secondary metabolites present like terpenoids, phenolic compounds, and polysaccharides, which possess antimicrobial and immunomodulatory properties (Lee et al., 2020; El Enshasy et al., 2013).

Finally, these results highlight the promising potential of truffles as sources of natural antimicrobial agents. While experimental studies' data are compelling, further research is needed to elucidate the exact molecular mechanisms, optimize extraction methods, and assess their safety and efficacy in clinical settings. Integration of truffle-derived antimicrobials into modern therapeutic paradigms could provide an innovative adjunct or alternative to conventional antibiotics, especially amid the rising threat of antimicrobial resistance (Lee et al., 2020; Taş et al., 2021).

### 5.3. Anticancer Activity

In this paragraph, the anticancer properties of truffles are described. In fact, most of the conventional antitumor drugs result in severe side effects, including immunosuppression and systemic toxicity. Such side effects can put the long-term efficacy of treatment at risk and hamper patient compliance with therapy (Talib & AbuKhader, 2013). Due to these drawbacks, there seems to be increased interest in new therapeutic methods using natural products that may not only enhance the effectiveness of therapy but also reduce toxicity (Talib, 2017). Studies in animals and cells have shown that edible fungi, particularly truffles, contain compounds that can interfere with immune pathways and slow tumor growth (here and here) in laboratory and animal models. (Wasser, 2002; Markman & Shiao, 2015).

Truffles contain bioactive polysaccharides and lipid-based compounds. *In vitro* and *in vivo* tests indicate that the extracted polysaccharides from truffles can inhibit cancer proliferation, suppress tumor cell migration, and stimulate immune-mediated anti-tumor activity (*in vitro*) (Friedman, 2016). These effects may involve activation of macrophages and lymphocytes, and enhanced production of immunoglobulins and cytokines (interferons and interleukins), which are critical for recognizing and eliminating tumor antigens (Moradali et al., 2007; Li et al., 2018).

Various scientific articles suggested that compounds isolated from truffles may improve immune surveillance *in vitro*. During tumorigenesis, genetic mutations generate neoantigens, but tumors can evade immune recognition through immunoediting. Truffle polysaccharides have been reported to bolster both innate and adaptive immune responses. Then it supports early immune recognition and limits tumor progression (Page et al., 2015; Aponte-López et al., 2018). These studies showed anti-mutagenic and anticarcinogenic potential of truffle extracts *in vitro* (Gajos & Hilszczańska, 2013). While these results are encouraging, it is essential to note that most of the available evidence comes from laboratory-based studies. These studies highlight the need for further research to confirm these effects and to translate the bioactive properties of truffles into practical clinical applications.

### 5.4. Immunomodulatory Activity

Truffles can also have potential immune-boosting effects in humans. Immunomodulation may be affected by Taneem factors, both external and internal (Shallal, 2025a, 2025b, 2026). Recently, truffles have attracted increasing scientific interest, as they are a rich source of secondary metabolites (e.g., polysaccharides, phenolic compounds, and terpenoids), which may modulate immune function. Among desert truffles, *Terfezia boudieri* is extensively reported as having a high content of bioactive compounds attributed to the immune-stimulating effects. *In vivo* preclinical work showed that *T. boudieri* extracts are able to modulate undirected and directed immune responses, supporting immunoregulatory capabilities (Al Obaydi et al., 2020).

Several studies indicated that truffle-derived compounds may exert immunomodulatory effects by regulating cytokine production. That led to increased macrophage activity and lymphocyte proliferation (Shallal et al., 2025). The fungal β-glucans (polysaccharides) and chitin-derived fibers isolated from truffles are thought to contribute substantially to these effects. Fungal β-glucans have been widely reported to exhibit immunostimulatory and hypolipidemic properties, primarily through interactions with immune cell receptors and modulation of inflammatory signaling pathways (Tejedor-Calvo et al., 2022).

*In vitro* studies demonstrated the immunomodulatory potential of truffle-derived compounds at the cellular level. Pressurized liquid extraction (PLE) extracts from *Tuber melanosporum* truffle have been shown to modulate the inflammatory response of human monocyte-derived macrophages differentiated from the THP-1 cell line. Moreover, these extracts were reported to attenuate lipopolysaccharide (LPS)-induced release of pro-inflammatory cytokines, suggesting a regulatory effect on excessive inflammatory responses (Tejedor-Calvo et al., 2020). Some studies have shown that compounds derived from truffles are able to balance immune activity, promoting appropriate immune responses without triggering excessive or uncontrolled inflammatory pathways.

In general, macrophages play a key role in host defense by producing cytokines, reactive oxygen species (ROS), nitric oxide (NO), and other mediators that help fight microbial infections. However, when macrophage activation becomes excessive, it can contribute to chronic inflammation and result in tissue damage. Truffle extracts appeared to influence this balance by modulating cytokines such as interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α). These cytokines are key mediators of the immune activation (Kong et al., 2014; Yao et al., 2016; Sun et al., 2017).

Finally, truffles have been used in traditional medicine to support health, enhance vitality, and strengthen immune defenses. Contemporary research supported these ethnomedicinal claims, demonstrating anti-inflammatory and immunomodulatory effects in both *in vitro* and *in vivo* studies (El Enshasy et al., 2013; Mustafa et al., 2020). Nevertheless, while these results are remarkable, current evidence remains largely from laboratory studies. Further studies focusing on compound isolation, mechanistic pathways, and clinical evaluation are required to establish the therapeutic relevance of truffle-derived immunomodulators in human health.

## 6. THERAPEUTIC AND NUTRITIONAL POTENTIAL OF TRUFFLES

Truffles are also famous from ancient times for both cultural and medicinal uses, mainly in Europe (Hilszczańska et al., 2014). Truffle production has developed considerably in the last years (also with the establishment of truffle farms in Poland during the 21st century), so their availability and accessibility are increasingly better (Hilszczańska et al., 2017; Rosa-Gruszecka et al., 2017). Several in vitro studies have shown anti-cholinesterase activity of some truffle species, but it has not been validated clinically (29–31), as well as differences compared with other dietary sources.

Truffles have been reported to exhibit antioxidant, antiviral, antibacterial, hepatoprotective, anti-inflammatory, and anti-mutagenic effects. These wide-ranging bioactivities have increased both their market appeal and potential therapeutic value. However, converting these biochemical and biological properties into functional foods or pharmaceutical formulations remains a major challenge and will require rigorous scientific validation (Rosa-Gruszecka et al., 2017; Hilszczańska et al., 2014, 2017, 2019).

Furthermore, truffles are reputed for their strong medicinal and edible properties. Truffle filth freak has values such as unique flavor, outstanding nutrition, and medicinal properties. They contain proteins, dietary fibers, lipids, essential amino acids as well as minerals and vitamins. They have been used as an ingredient in many delicious plates, especially in European recipes (Üstün et al., 2018). In addition, truffles contain a variety of bioactive substances with potential therapeutic effects such as antioxidant, antimicrobial, anti-inflammatory, hepatoprotective, antidepressant, aphrodisiac and anticancer properties (Lee et al., 2020; El Enshasy et al., 2013).

Truffles are symbiotic with host plants in the wild and produce distinct metabolites that vary between species. These metabolites are terpenoids, polysaccharides, phenolic compounds, and volatile organic compounds (VOCs) such as ketones, aromatic hydrocarbons, alkenes , including sulfur-containing compounds. The above compounds are, together, responsible for the characteristic odor of truffles and their (biological) activity as well (Strojnik et al., 2020). The type and quantity of these bioactive compounds differ based on the types of truffles, as well as its maturity stage, and the environmental conditions in which they are grown (Lee et al., 2020).

The medicinal properties of desert truffles are reported in the ethnopharmacological literature of North African and Middle Eastern traditions. The desert truffles have been used as aphrodisiacs and as remedies for ocular conditions (El Enshasy et al., 2013; Mandeel & Al-Laith, 2007; Alrhmoun et al., 2025). Many studies support these traditional claims, demonstrating that truffle extracts possess antibacterial activity toward *Staphylococcus aureus*, *Escherichia coli*, and *Staphylococcus epidermidis*, with potential applications in ocular and systemic infections (Janakat et al., 2004b; Casarica et al., 2016a; Owaid et al., 2018). Moreover, truffles exhibited antiviral effects and have been implicated in modulating immune responses (Gajos & Hilszczańska, 2013).

The effect of this system on both sensory and potential physiological effects is suggested to be due, at least in part, to the presence of a number of bioactive compounds in truffles [e.g., androstanol (a steroidal pheromone)], which influence attraction/sexual behaviour in animals. Several reports also indicate that other roles should be played by truffle metabolites in the ecology, and may have promising perspectives in pharmacological applications (Al-Damegh, 2014; Akyüz et al., 2012; Lee et al., 2020). For these reasons, interest in using truffles in pharmaceutical and cosmetic products is supported not only by their nutritional content but also by their bioactive properties. Reported benefits include immune support, cholesterol-related effects, antioxidant protection, and possible contributions to neurological health (Lee et al., 2020; Gajos et al., 2014).

## 7. SAFETY AND TOXICITY CONSIDERATIONS

The capacity of a compound to damage or kill viable cells is a critical measure in evaluating potential toxic effects of natural products. *In vitro,* cytotoxicity assays employ diverse cell lines and endpoints, including cell morphology, proliferation, metabolic activity, and viability (Damas et al., 2011; Kasper et al., 2011; Piao et al., 2011; Osthues et al., 2012; Uboldi et al., 2012; Soloneski & Larramendy, 2021). For truffles, several studies have begun to elucidate their cytotoxic profiles. For instance, a water-soluble heteroglycan from *Tuber rufum* stimulated lymphocyte activity and redox balance without evident toxicity (Pattanayak et al., 2017). Also, the methanolic extracts of *T. claveryi* administered to rodents showed no observable adverse effects (Dyary, 2020).

Generally, *in vitro* studies indicate that high concentrations of certain truffle extracts, such as *Tirmania nivea,* may exert cytotoxic effects on Hep-2 cells, suggesting a dose-dependent relationship that warrants careful evaluation (Ibrahim et al., 2011; Hateet & Muhsin, 2020). Finally, these findings indicate that truffles are generally low in toxicity at conventional doses. Still, further systematic investigations-including standardized *in vitro* assays, experimental toxicology studies, and controlled human studies-are essential to ensure their safe integration into functional foods or therapeutic formulations.

## 8. CONCLUSION

This study is a review of the dietary and therapeutic aspects of truffles. Truffles are specialized edible fungi fruiting below ground and with high culinary value. Apart from their taste, they are also good sources of several multi-bioactive compounds such as polysaccharides, terpenoids, phenolic compounds, including sterols and volatile organic constituents. Numerous previous researches have been conducted about antimicrobial, antioxidant, anti-inflammatory, immunomodulatory , and anticancer effects of truffles. They are also high in proteins (including amino acids), dietary fiber, and essential minerals that may benefit general health, along with reducing the risk of life-style related diseases. In recent times, silver nanoparticles synthesized from desert truffles have shown good antibacterial and antifungal activity. Nevertheless, despite these promising results, their use in clinical practice is still limited by the absence of studies performed in human beings and incomplete toxicological assessments, also concerning differences between truffle species as well as a lack of knowledge on the biological mechanisms behind their medicinal properties.

### Ethical Statement

Not Applicable.

### Conflicts of Interest

The authors declare no competing interests.

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