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Food Additive Evidence in Food Supplements Most Commonly Consumed by Cancer Patients

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Cover Page Footnote

We would like to thank all the medical and paramedical staff as well as the patients of the center for the fight against cancer in the wilaya of Annaba who contributed to this study.

FOOD ADDITIVE EVIDENCE IN FOOD SUPPLEMENTS MOST COMMONLY CONSUMED BY CANCER PATIENTS

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ABSTRACT

The goal of this research is to highlight food additives in the formulations of food supplements consumed by cancer patients. It is a survey conducted at the Cancer treatment center in Annaba to collect a list of food supplements used by these patients. Following a screening of their ingredients for incorporated food additives, which we then classified according to the degree of toxicity, these supplements were classified according to their origin (local or imported). Our findings show that these various groups of dietary supplements contain a variety of food additives with varying degrees of toxicity, such as colorants (E422), acidity regulators (E330), preservatives (E202), stabilizers (E420i), emulsifiers (E322), conditioning agents (E460), thickeners (E441), and so on.

Keywords: Cancer, food additives food supplements, toxicity, patients.

INTRODUCTION

One's health, emotional well-being, stress levels, fatigue, physical appearance, and more all warrant consideration. Nutritional supplements are non-pharmaceutical substances that offer a nutritional or physiological benefit (Harvie, 2014). They are essential to address any potential deficiencies that could negatively impact the body's overall health and enhance one's quality of life, particularly for individuals with heightened sensitivities.

As a result, cancer patients obtain these nutritional supplements with the goal of avoiding disease aggravation and improving their lifestyle by minimizing the side effects of treatments such as chemotherapy and radiotherapy.

However, some supplements may have negative side effects (Larsson et al., 2010; Poljsak and Milisav, 2018). The most concerning are those that may reduce the effectiveness of certain cancer treatments or cause other effects, especially if taken for an extended period of time.

This study aims to highlight the inclusion of food additives in the formulations of food supplements consumed by this group of patients, despite the fact that they are very sensitive and immunocompromised, which can result in an opposite effect and thus jeopardize their remission.

METHOD AND MATERIAL

It is a survey conducted at the Abdelaziz Al Saoud Cancer Center (CAC), Ibn Rochd University Hospital, Annaba, Algeria; Algeria, to collect a list of food supplements consumed by 250 cancer patients. A questionnaire was created with the patients' first and surnames, as well as the dietary supplements they used during their cancer treatment. Then we went to

several pharmacies and Para-pharmacies to obtain these food supplements.

Our research lasted three months: February, March, and April. Our survey was conducted between 10 a.m. and 3 p.m. to collect data on each product.

We investigated the various supplement classes and forms (syrup, ampules, capsules, powdered bags, candies, etc.) available. The boxes and leaflets of the products mentioned by the patients during our survey were selected and listed, and photos were taken with a cell phone focusing on the following content:

- The product's commercial name and place of manufacture
- The product's composition or list of ingredients
- The product's use (classes).

The data was registered in an Excel spreadsheet. The food additives were then highlighted in the ingredient list. In total, 181 food supplements were divided into seven categories: dietary complements for skin, hair, and nails; anti-stress and sleep aids; vitamins, minerals, and trace elements; beehive products; probiotics and spirulina; food supplements for memory, concentration, and appetite; and nutritional supplements for other health issues (Table 01). We used excel for the statistical analyses for our study.

RESULTS

Table 01 categorizes food supplements according to their origin. We gathered 35 domestic and 146 imported items. Patients prefer imported food supplements to local ones.

Figure 01 shows that the most consumed dietary supplements contain 7 categories of food additives in varying proportions: 727 food additives are highlighted. The following are the most common additives:

Figure 02 shows that colorants and thickeners are in first place with the same proportion of 17 %, followed by emulsifiers and acidifiers with 16 %, sweeteners with 13 %, antioxidants with 6 %, coating agents and preservatives with 4 %, and anti-caking agents with 3 %. Finally, the least commonly used additives are present in the same proportion of 1 %: acidity regulators, humectants, flour treatment agents, and color retention agents.

Figure 03 shows that dubious additives are the most common in the formulation of local food complements, accounting for 47 % of the total (E572, E553). Toxic additives (E460) and not to be abused (E330) come in second and third with 23 % and 17 % respectively. At 12 %, the low or non-toxic additives (E300, E530) come next. Finally, very toxic additives (E133) with a very low value of 1 % have been identified.

Table 1: Distribution of the most commonly consumed food supplements by cancer patients according to class and origin (local and imported).

Food supplements classes	Local	Imported
Memory and concentration	5	21
Antistress, fatigue and sleep	11	33
Probiotics and spirulina	0	4
Skin, hair and nails	0	15
Health problems	6	27
Vitamins, minerals and oligo-elements	9	41
Hive products	4	5
TOTAL	35	146

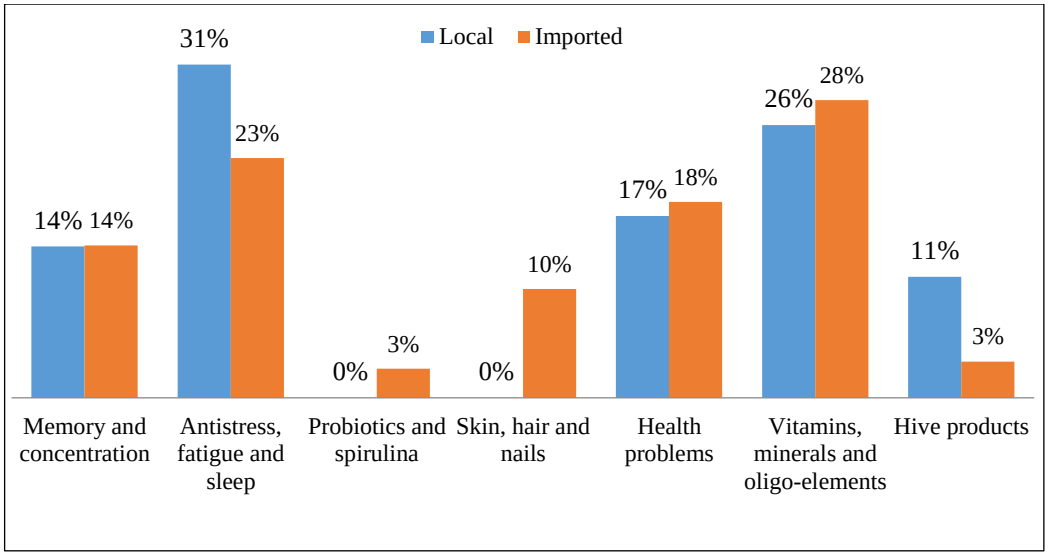

Figure 01: Distribution of dietary supplements most commonly consumed by cancer patients by class and origin (local and imported).

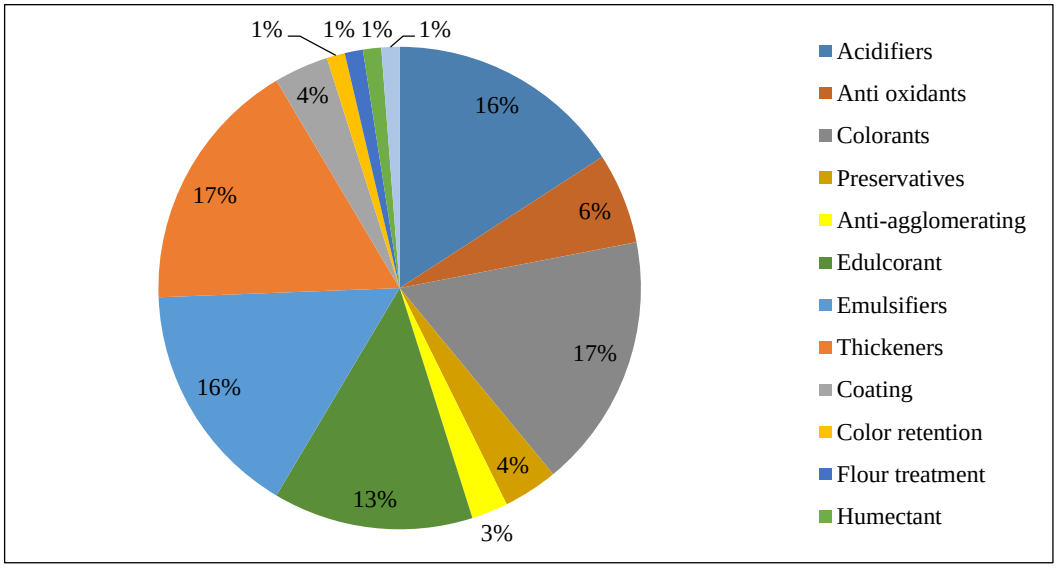

Figure 02: Distribution of food additives found in collected food supplements (local and imported) according to their function.

Figure 04 summarizes the levels of food additives in imported nutritional supplements. With a value of 44 %, the dubious additives (E420, E551, E572) are the most commonly used.

Following that are harmful additives (E422, E330, E322) with a value of 19 %. Then there are the Toxic (E460, E171) and Low/Non-toxic (E300, E530, E306) additives, each with an 18 %. Finally, the most toxic additives (E122) are the least common, accounting for only 1 % of the total value.

According to the results (Figure 05), the food additives listed in the food supplements of "local and imported" origin are classified based on their degree of toxicity, and we discovered that "Dubious" additives are the most commonly encountered, with a rate of 47 % in local products and 43 % in imported products. Additives "Not to be abused" account for 19 % of imported food supplements and 17 % of local products, respectively, while "Toxic" and "low /not toxic" additives account for 18 % of imported dietary complements and 23 % and 12 % of local products, respectively.

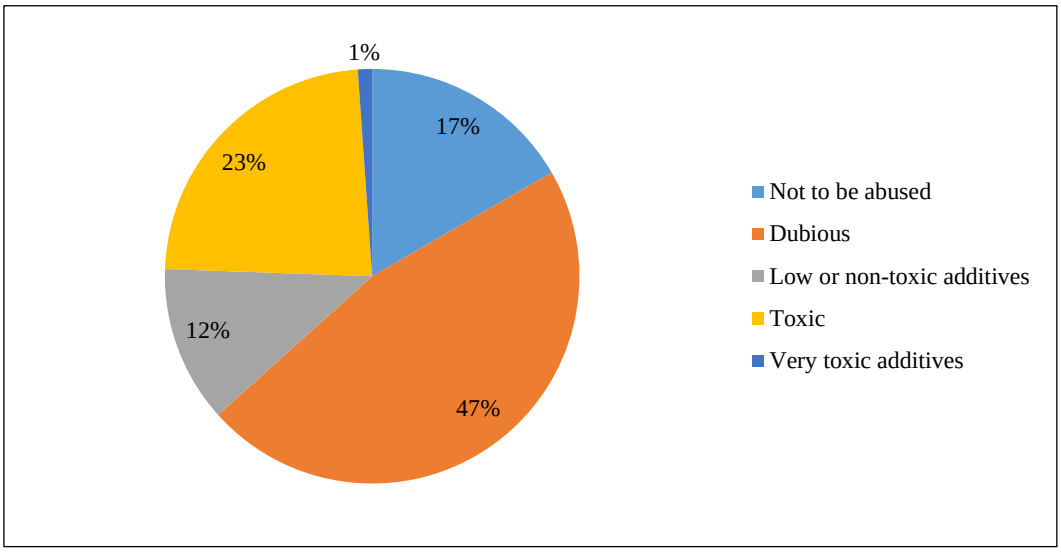

Figure 03: Distribution of food additives in local dietary supplements for cancer patients based on toxicity.

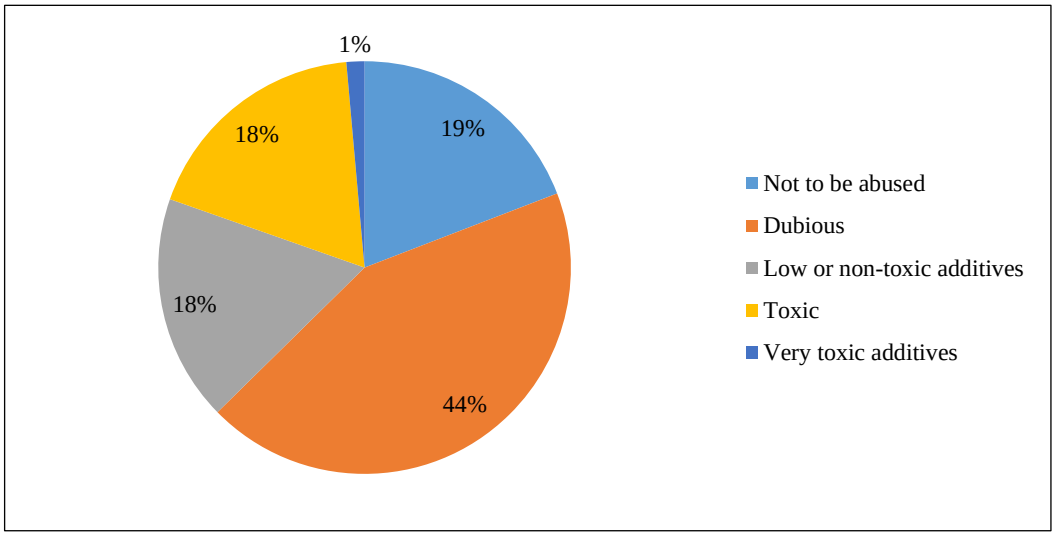

Figure 04: Distribution of food additives in imported dietary supplements for cancer patients based on toxicity.

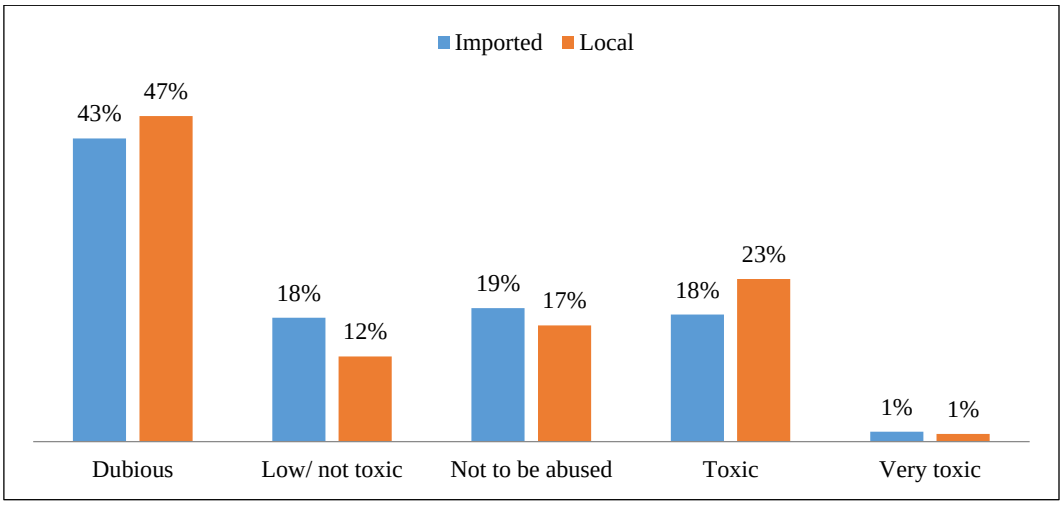

Figure 05: Toxicity distribution of food additives.

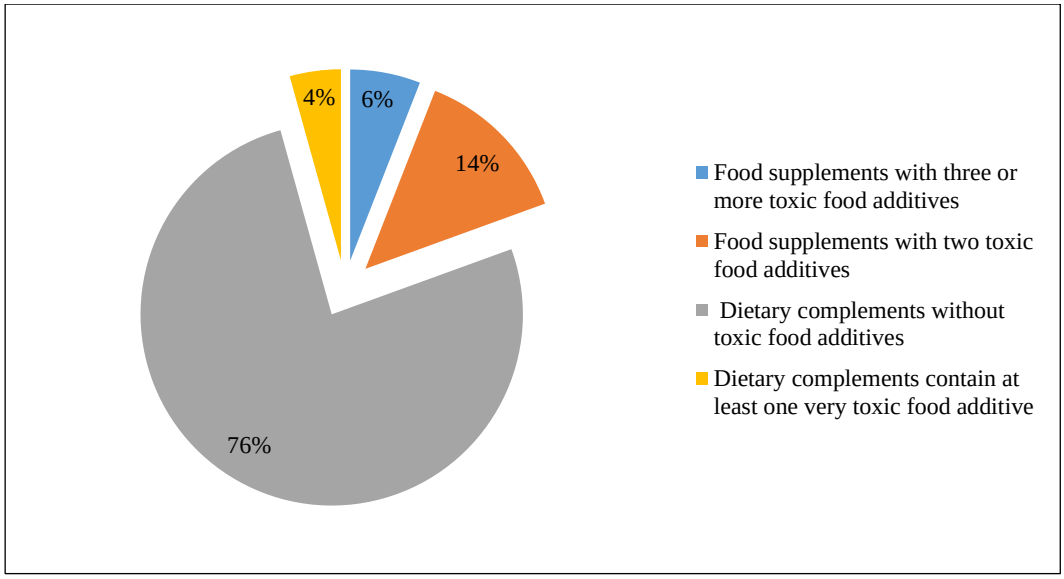

Figure 06: Food supplement distribution based on the presence of carcinogenic food additives in their formulation.

It can be seen (Figure 06) that 14 % of food supplements contain at least two toxic food additives in their composition; additionally, 6 % contain three or more toxic food additives in their composition; and finally, 4 % of dietary complements contain at least one very toxic food additive in their formulation. However, additives are only present in trace amounts in probiotics, spirulina, and beehive products.

DISCUSSION

Nowadays, it is very common for patients to take an increasing number of nutritional supplements. Cancer patients are not excluded. In comparison to other global markets, the food supplement industry entered the Algerian market late. However, products of imported origin are widely available and, as a result, widely consumed. This is supported by our survey results, which show that very vulnerable patients, such as cancer patients, consume 81 % of imported products and only 19 % of local supplements (see Figure 01).

In nutritional supplements, we found 727 different food additives. Some of them are suspected of endangering consumer health. This estimate may vary depending on the subject's physiological state and, in particular, the acceptable daily intake. To assess our findings, we classified the most frequently discovered food additives into five categories based on their toxicity: not very toxic, not to be abused, doubtful, toxic, and very toxic.

Among the suspect additives was magnesium stearate (E572), an anti-caking agent added to dietary complements to prevent lump formation (Tebbey and Buttke, 1990). Because of the scarcity of studies on its toxicity, researchers are skeptical of its effects.

In 1980, a study (Søndergaard et al., 1980) discovered that 2500 mg of magnesium stearate/kg of body weight is the maximum amount a person can absorb without experiencing negative effects. In addition, (Hobbs et al., 2017) suggest that further research may be needed to assess the potential health effects of long-term exposure to various sources of magnesium contained in food additives.

In contrast, another study (Evans et al., 2009) claimed that E572 can prevent breast cancer cells from migrating and invading as well as initiate apoptosis. However, the specificity of this phenomenon towards cancerous and non-cancerous breast cells has yet to be

explored. Moreover, the mechanism responsible for stearate-induced apoptosis remains unclear.

A recent study (Hobbs et al., 2017) found no risk of geno-toxicity from magnesium stearate consumption. These studies lead us to the conclusion that this additive is still questionable.

As a result, more research is needed to investigate its long-term toxic effects on health. It is therefore critical that cancer patients are aware of the potential dangers of these substances before taking dietary supplements containing this substance (E572). The most commonly used questionable additive in local food supplements is magnesium silicate (E553).

This additive's use in tablet formulations has not been shown to be hazardous when consumed. Indeed, no adverse effects have been observed when this additive is ingested orally, according to Hollinger (1990) and the US EPA (1992). According to the EFSA Panel on Food Additives and Nutrient Sources in Food (EFSA, 2018), no human studies on magnesium silicate have been conducted. Furthermore, there has been no research into how this additive is absorbed, distributed, metabolized, or excreted. Indeed, no formal studies on the toxicity of E553 have been conducted (The EFSA Panel on Food Additives and Nutrient Sources Added to Food (ANS), 2018).

Then there's citric acid (E330), a dangerous additive that's frequently found in both domestic and imported CA. It should not be used in excess. According to one study, a high dose of this additive can cause nephrotoxicity in rats (Chen et al., 2015). On the other hand, according to a study on the effect of citric acid on blood coagulation (Scaravilli et al., 2018), the latter can be influenced by citric acid infusions.

Even in large quantities, ascorbic acid E300 is not considered toxic (Gouget, 2014). When added to food, it is considered a potent source of vitamin C. It is the most common additive in the composition of local and imported food supplements. Because ascorbic acid is permitted as an antioxidant in food, no additional evidence of efficacy was deemed necessary. The EFSA concluded that there were no safety concerns with the use of ascorbic acid E300 (EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), 2013).

Long-term consumption of large amounts of E300, on the other hand, can cause gastrointestinal disorders, particularly nausea and diarrhea, as well as affect urinary function. (2018 Sordalab safety data sheet, version 1.2). As a result, high doses of this additive may be harmful to the health of patients.

In terms of toxic food additives present in imported and local dietary supplements (used as a thickener, bulking agent, and carrier for additives), cellulose (microcrystalline E460i and powdered cellulose E460ii) ranked first. Despite contradictory research, this food additive was declared carcinogenic in 1961 but is still permitted (Gouget, 2014).

However, according to the EFSA report, E460 has a low acute oral toxicity (EFSA, 2009a, b, EFSA CONTAM Panel, 2009, 2010, 2012).

In 2018, an unpublished study showed an increase in body weight, liver weight and kidney weight in male rats receiving microcrystalline cellulose gel and dystrophic calcifications in the renal tubules of females receiving (E460i) (Documentation provided to EFSA no. 40). (EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), 2018). Nevertheless, the latest EFSA paper (EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), 2018), determined that cellulose does not cause genotoxicity or carcinogenic properties. They also stated that modified celluloses have no negative effects on human health.

Following the contradictory findings on the toxic effect of E460, patients should consult their primary care

physician before taking any dietary supplements containing these compounds to ensure their safety and well-being.

According to Gouget (2014), Brilliant Blue FCF (E133) is toxic and ranks first among toxic food additives used in the formulation of locally sourced CA. It is a blue dye that has been synthesized. For health-conscious consumers, the toxicity of food coloring, particularly brilliant blue FCF, is a major concern. Indeed, E133 has been linked to a variety of negative effects, including an increase in total serum lipids, cholesterol, and triglycerides, as well as a decrease in hemoglobin concentration (Aboel-Zahab et al., 1997).

However, studies have shown that it is not as safe as it appears, particularly if the ADI is followed. The EFSA Scientific Panel set the acceptable daily intake (ADI) for this additive at 6mg/kg body weight/day in 2010. Furthermore, it stated that, even if its use in small quantities is approved, it is critical to understand the potential risks associated with FCF Brilliant Blue, which can cause hypersensitivity reactions in vulnerable individuals (EFSA, 2010). Other studies have found that this dye causes changes in neurobehavioral parameters in mice over multiple generations (Tanaka et al., 2012), as well as cytotoxic and genotoxic effects on certain human cells (lymphocytes) (Kus and Eroglu, 2015).

The most common additive in imported dietary supplement formulations consumed by cancer patients is sorbitol/sorbitol syrup E420i (ii). It is a questionable sweetener and humectant due to a lack of studies proving its toxicity (Gouget, 2014). This additive has sweetness similar to sucrose and is used in the production of light products. Although it is not as easily absorbed as sucrose, it is metabolized to produce glucose. As a result, it is high in calories (2.4 kcal/g) and raises blood sugar levels moderately, both of which are disadvantageous for diabetic cancer patients and those who are overweight (Amouyal and Andreelli, 2012). In fact, this can cause hyperglycemia and make chemotherapy less effective.

When taken in large quantities, sorbitol can cause diarrhea, bloating, and abdominal pain. Although these symptoms appear to be innocuous, they can exacerbate the side effects of chemotherapy, which can cause dehydration and electrolyte imbalances, worsening cancer patients' already compromised condition.

Indeed, some scientific studies have found more harmful effects, such as decreased absorption of vitamin B6, which is required for proper muscle function (Gouget, 2014). What about the long-term effects, especially in vulnerable groups, given that these are the short-term effects.

E551 Silica (amorphous) or silicon dioxide (amorphous). Due to the lack of toxicological studies, this anti-caking agent is considered suspect (doubtful) in imported CA. Nonetheless, some sources claim that this additive contains nanoparticles, the risks of which are unknown (Gouget, 2014).

Furthermore, it induces dose-dependent changes in ROS responsible for cytotoxicity and even modifies gene expression and the cell cycle, according to the findings of (Athinarayanan et al., 2014).

Aouey et al., 2022, on the other hand, published a study evaluating the effects of prolonged and repeated exposure to amorphous silica nanoparticles. The study discovered that mice given doses of 25 and 100 mg/kg body weight caused liver inflammation and histological abnormalities in the kidneys. Furthermore, recent research has found that SiO2 particles have a low potential for DNA damage (Dussert et al., 2020).

The findings of (Boukholda et al., 2021) revealed a variety of negative effects following SiO2 exposure in rats, including inflammation, oxidative damage, and hippocampus alterations. Furthermore, the

rats displayed signs of cognitive and behavioral decline. However, according to the EFSA Panel (2018), the EU criteria are insufficient to adequately and definitively characterize E551. Due to the limitations of the available databases, the scientific panel is unable to confirm the acceptable daily intake because there is no evidence that this additive is harmful, according to EFSA. Based on previous research, it is possible that this additive (E551) could be toxic to cancer patients whose immune systems have already been weakened by chemotherapy treatments.

E422 Glycerol or Glycerin: a filler/humectant found in the first line of nutritional supplements that should not be used in imported food complements. They occur naturally in fats and oils (Gouget, 2014). A bioassay performed in rodents with 10 % glycerol revealed no toxic or teratogenic effects (Dalla Vedova et al., 1976). However, in high doses, this additive can cause unpleasant sensations such as nausea, thirst, and even hypertension (Gouget, 2014). It is thus not advised for subjects with sensitive health conditions, such as cancer patients, because the ability of foods containing glycerol (E422) to form toxicologically harmful components under certain processing conditions (recommended in the EFSA re-evaluation of E422) has not been clarified (EFSA Scientific Panel SNA, 2017; EFSA, 2022).

Finally, the highly toxic food additive (E122) azorubin or carmoisine is the most commonly found in the composition of imported CA. It is a synthetic red coloring agent that is mostly found in charcuterie and is prohibited in Australia, Norway, Sweden, and the United States (Denans, 2017). According to Gouget (2014), this additive is carcinogenic and can result in hyperactivity, skin reactions, allergies, and insomnia, among other things. In this survey, we also discovered a number of supplement categories that do not comply with regulations, leaving consumers perplexed.

The combined or cocktail effect of toxic food additives is a topic that deserves further investigation. In our study, we discovered that 14 % of supplements contained two toxic food additives and 6 % contained three or more toxic nutritional additives. Interactions between these additives can also have negative consequences. Certain substances can react to form hazardous chemical compounds that are harmful to one's health. In fact, combining these toxic substances in the same supplement may increase the product's toxicity and make it more dangerous.

In his book *Le nouveau guide des additifs*, author Denans (2017) stated that in the presence of the brilliant blue colorant (E133), BHA (E320) increased pulmonary toxicity when combined with BHT (E321). Similarly, Gouget (2014) claims in his book Food Additives that when the brilliant blue color E133 is mixed with monosodium glutamate (E621), it becomes four times more harmful to health, especially for sensitive individuals. Some cancer patients are unaware of the effects of this combination of harmful additives, which could lead to increased toxicity or undesirable interactions with anti-cancer treatments, thereby impeding or jeopardizing their recovery.

CONCLUSION

The impact of nutritional supplements on cancer patients is extremely complicated due to the numerous factors that must be considered. It's critical to understand both the potential benefits of nutritional supplements and the risks and side effects of their various food additives. Numerous studies on the consumption of nutritional supplements by susceptible subjects have been conducted, with some demonstrating potential benefits such as improved quality of life, lower

levels of toxicity, and increased survival rates. However, very little research has been conducted to determine the true effectiveness of these nutritional supplements on the health of cancer patients. More research is needed to fully understand the benefits and risks associated with these products.

In comparison to imported products, the results show a slightly exaggerated incorporation of toxic and dubious food additives in local products. It appears that imported supplements are of higher quality than locally produced supplements. The majority of the additives used in these supplements, whether local or imported, are questionable.

There are numerous avenues open for researchers to investigate the effects of food supplements on health and the long-term consequences of consuming them, particularly in terms of cancer risk, but researchers are encountering methodological challenges relating to the form, dosage, and duration of intake, which appear difficult to assess and study.

Several factors must be considered when determining the best dietary supplement for these patients. Some supplements may interact with one another or even with anti-cancer medications (as mentioned in the discussion).

Furthermore, certain supplements may have an effect on the metabolism of specific drugs taken concurrently.

Moreover, some food supplements may contain substances that should not be consumed in large amounts, such as dubious additives.

To ensure safety, it is best to consult a healthcare provider before taking supplements containing food additives, as there may be risks involved. It is crucial to bear in mind that there is no definitive answer regarding the correlation between food additives and cancer.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

All authors participated in the drafting and critical review of the manuscript.

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