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Evaluation of Titanium Dioxide Levels in Certain Traditional Food in the West Bank

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الإقرار

أنا الموقع أدناه مقدم الرسالة التي تحمل العنوان:

Evaluation of Titanium Dioxide Levels in Certain Traditional Food in the West Bank

أقر أن ما شملت عليه هذه الرسالة أنما هو نتاج جهدي الخاص، باستثناء ما تمت الإشارة إليه حيثما ورد، وان هذه الرسالة ككل أو جزء منها، لم يقدم من قبل لنيل أي درجة أو لقب علمي لدى أي مؤسسة تعليمية أو بحثية أخرى.

Declaration

The work provided in this thesis, unless otherwise, referenced is the researchers own work, and has not been submitted elsewhere for any other degree or qualification.

Student name: othman Awni Khalil Daher

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Date: 16/10/2018

Dedication

I dedicate this thesis to the most important people in my life "my parents" who always have encouraged me to pursue science, progress, acquire knowledge, and gave me hope and strength to complete this work.

To my wife who helps and supports me, and to my children who give me hope and a beautiful future.

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List of Abbreviations

- **ACGIH**: The American Conference of Governmental Industrial Hygienists.
- **Al_2O_3:** aluminum oxide.
- **AF4-ICPMS:** asymmetric flow field-flow fractionation with inductively coupled plasma mass spectrometry.
- **2B:** possibly carcinogenic to humans.
- **º c**: Celsius degree.
- **Cr_2O_3**: chromic dioxide.
- **CECs**: Contaminants of emerging concern .
- **DNA:** Deoxyribonucleic acid.
- **DNFCS**: The Dutch National Food Consumption Survey.
- **EU**: European Union.
- **EFSA**: European Food Safety Authority.
- **EDCs**: Endocrine disrupting compounds.
- **FDA** : Food and Drug Agency .
- **FPs**: fine particles.
- GOs: governmental organizations

- **g/mol: gram** per mole.
- **g/cm3:** gram per centimeter cubic.
- **gr**: gram.
- **H_2SO_4**: sulfuric acid.
- **IARC**: The international agency for research on cancer.
- **IFIC**: International Federation of Infection Control.
- **ICP-MS**: inductively coupled plasma mass spectrometry.
- **ISO:** the International Organization for Standardization.
- **ICPOES:** inductivity coupled plasma optical emission spectrometry.
- **mg / kg:** milligram per kilogram.
- **µg/L:** microgram per litter .
- **mg/kg bw/d** : milligram per kilogram of body weight per day .
- **mg/g** : milligram per gram .
- **MoS** : the margins of safety.
- **NGOs :**non-governmental organizations.
- **No: number of**

- **NOAEL**: the no observed adverse effects levels.
- **NPs**: nano particles .
- **OSHA:** the Occupational Safety & Health Administration.
- **PSI: Palestine** standards institution.
- **PSM:** The Palestinian Standards Mark .
- **PMOH**: The Palestinian Ministry of Health.
- **PPM** :part per million = mg/kg
- **PEL**: Permissible exposure limit.
- **PhCs.** : pharmaceutical compounds .
- **PCPs** : Personal care products .
- **PW6** : Pigment White 6 .
- **SC**: stratum corneum .
- **SiO_2 :**silicon dioxide .
- **SEM**: scanning electron microscopy .
- **sp-ICPMS**: single particle ICPMS.
- **SEM**: scanning electron microscopy .
- **TLV**: a threshold limit value .

- **TWA** : a time weighted average .
- **Ti**: Titanium.
- **TiO_2** :Titanium dioxide.
- **$TiCl_4$**: Titanium tetrachloride.
- **TiO_2-NPs**: Titanium dioxide nanoparticles.
- **TDMA** : The Titanium Dioxide Manufacturers Association .
- **UV**: Ultra Violets rays.
- **UVA/UVB :**Ultra Violets (A,B) rays.
- **US**: United State.
- **UK**: United Kingdom .
- **WWTPs**: waste water treatment plants.
- **W/W:** Weight by Weight

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Abstract

Titanium is a bleaching substance used as a food bleach and a Category 2B carcinogen. Despite Titanium dioxide (TiO_2) has been banned as food additives since 2015 by standard and measurement authority and Palestinian health ministry, it is still used especially in popular food such as humus, tahini, and halawa. Titanium dioxide in Palestinian food could be a health concern and the evaluation of the risk of Titanium dioxide is required. The objectives of this research was to establish the levels of Titanium dioxide in the most popular Palestinian food humus, tahini, halawa, and egg plants appetizer in the years 2005-2017 and to compare the levels of TiO_2 before and after it was banned in these food. Titanium dioxide was tested in 444 samples of different types of food, halawa, tahini, humus, and egg plants appetizer from the year 2005 to 2017 by Palestinian Ministry of Health (PMOH) and in Birzeit University (Centre for Testing Laboratories). Out of the 444 food samples tested, 207 samples (46.4%) had shown a concentration of TiO_2 more than the legalized concentration (0 mg/kg). The majority of the samples (90.3%) were originally from the West Bank and only 42 (9.5%) were from Egypt and 1 (0.2%) from Turkey. TiO_2 was detected in 46.6% of the samples and

(61.9%) of samples from Egypt had TiO_2. TiO_2 was detected in 53.6% of Halawa samples, 48% of Humus samples, and 37.3% of Tahini samples. All types of food tested have high levels of TiO_2 and ranged (2-5400) mg/kg and even after the year 2015 when it was banned by Ministry of Health (MOH). Small projects funded by NGOS and restaurants are the most source of TiO_2 in food. The findings of this study indicate that TiO_2in the popular Palestinian food present a serious threat to current and future health of Palestinian. More regulation and monitoring is needed and law enforcement is required. More research is needed to explore possible risk of these of TiO_2 in order to establish specific direction of prevention strategies.

Chapter One

1.1. Introduction

1.1.1 Chemical and Physical Properties of Titanium

Titanium (Ti) is one of the most abundant and spread elements on the surface of earth crust and lithosphere where levels are around 4400 mg/kg (Organization, 1982b). It is found in almost all living things, water bodies, rocks, and soils (Enoch and bin Ismail, 2012). It is non-magnetic and a poor conductor of heat and electricity. Titanium exists in different forms combined with other minerals. The most common oxidation state of Ti is $^{+}4$, but $^{+}3$ and $^{+}2$ states are also found in nature.

Titanium (Ti), Titanium dioxide (TiO_2), and Titanium tetrachloride ($TiCl_4$) are the most widely used element compounds in industry (Shon et al., 2007). Titanium dioxide is a poorl10y soluble particulate, a white noncombustible, crystalline, solid and odorless powder with a molecular weight of 79.9 g/mol, boiling point of 2972°C, melting point of 1843°C, and relative density of 4.26 g/cm^3 at 25°C.It is used as a pigment and the majority of the TiO_2 pigments used in consumer products is being extracted from ilmenite ore ($FeTiO_3$) and leucoxene ore (TiO_2_xFeO_yH_2O), either by sulfate or chloride processing (Dambournet et al., 2009, Jovanović, 2015). Titanium dioxide which has a chemical abstract service-No. 13463-67-7), also known as Titanium (IV) oxide, titanic acid anhydride, titania, titanic anhydride, or Ti white, is the naturally occurring oxide of Ti (Chen and Mao, 2007, Warheit et al., 2007)

Annex 2. Physical and chemical characteristics of Titanium dioxide are shown in Annex 1.

1.1.2. Uses of TiO_2

Titanium dioxide is used every day in our life (Skocaj et al., 2011a). It has been used in many applications for decades. It is increasingly manufactured and used. Therefore increased human and environmental exposure can be expected, which has put TiO_2 nanoparticles under toxicological scrutiny (Skocaj et al., 2011a).

In food, Titanium dioxide has different uses. Its food-grade form is used as a colorant to enhance and brighten the color of white foods such as dairy products, candy, icing, and as powder that is used in bakery such as on donuts (Weir et al., 2012). In Arabic countries, it is used to whiten certain types of food such as tahini and halawa. Therefore, it is found these many food types use tahini such as humus and other appetizers such as (Mutable). Most of these products are used daily by Palestinians. It is also used in different products that is used by adults and children such as drinks, ice cream, and chewing gum. These products are daily used by children.

For foods that are sensitive to UV light, Titanium dioxide is used for food safety purposes to prevent spoilage and increase the shelf life of food (Skocaj et al., 2011b) .

In cosmetics products, TiO_2 is used in sunscreen as effective protection against UVA/UVB rays from the sun, which creates a physical barrier between the sun's rays and the skin. Its penetration to skin is low and therefore, it is considered safe (Skocaj et al., 2011b). It is also used to whiten paint, paper, plastic, ink, rubber, and cosmetics. It is used for removal of arsenic in treated water (Bang et al., 2005).

Although TiO_2 is permitted as an additive (E171) in food and pharmaceutical products we do not have reliable data on its absorption, distribution, excretion and toxicity on oral exposure. TiO_2 may also enter environment, and while it exerts low acute toxicity to aquatic organisms, upon long-term exposure it induces a range of sub-lethal effects (Skocaj et al., 2011a).

1.1.3. Foods Contain Titanium Dioxide

Many popular consumer products such as candies, gum, and baked goods contain 0.01 to 1 mg TiO_2 per serving. Generally, products with the highest Titanium contents are sweets, chewing gums, confectionaries, chocolates and candies (Chen et al., 2013). Powdered donuts can contain up to 100 mg Ti per serving which mean 2 mg/g food while nestle original coffee creamer had the a content of 0 .93% mg/g food (Weir et al., 2012).

1.1.4. Source of TiO2 in Palestine

The amount of food-grade Titanium dioxide that is used in many countries is small. The FDA has set a limit of 1 percent Titanium dioxide for food (Heringa et al., 2016). Many food factories and food restaurants in Palestine use TiO_2 in food processing as food additives (E171) to enhance color, texture and increase shelf life of products (Rydström, 2012). Some food factories and restaurant used TiO_2 without knowing the limitation of application, and if its banned or not. Titanium dioxide in products is still used especially in popular food such as humus and tahini, halawa, and egg plants appetizer with higher concentration (Rydström, 2012).

1.1.5. Legalization of TiO2 NPs

International Agency for Research on Cancer (IARC) did not assess the effects of Titanium dioxide found in foods. The European union allows TiO_2 in its food products in most cases at quantum satis level, with an exception of some products listed in food additives data base, which not allowed at all (European parliament 1994). In Egypt, the ministry of health and housing issued law no .114 on January 3rd 1979 banning the use of Titanium dioxide as coloring or bleaching agent for tahini sauce (alosra, 2017). In Jordan, the standard and measurement authority, in its session number 01/3002 held on Novembers 21, 2003, agreed to implement law no .56/2003 to ban the use Titanium dioxide in tahini and other products by The General Organization for Food and Drugs, Jordan (ARIJ, 2013). The Saudi Arabia standards and measurement authority banned the addition of Titanium dioxide as bleaching agent to tahini souse in 1973 in accordance with law no .693/73 (ARIJ, 2013). In Palestine, the standard and measurement authority monitored the use of Titanium dioxide at 2013 and banned it at 2015. (ARIJ, 2013). Although Titanium dioxide has been banned as food additives since 2015 by standard and measurement authority and Ministry of Health (MoH), Titanium dioxide in products is still used especially in popular food such as humus, tahini, halawa. Moreover, no information about the content of TiO_2 is written on the food product label. With a likely intake of TiO_2NPs and recent indications of their toxic effects, it is relevant to assess whether this exposure can lead to health risks.

Based on the previous information, Titanium dioxide in food could be a health concern and the evaluation of Titanium dioxide risk is required.

1.2. Objectives

1.2.1. General objective

This study aimed to evaluate the use of TiO_2 in the certain traditional food in Palestine in order to assess the risk of using it in different concentration in the popular food. Specifically, TiO_2 concentrations will be assessed in different popular food, from different governorates, from different products and sources of the manufactured companies.

1.2.2. Specific objectives:

The objectives of this research were:

1. To determine Titanium dioxide levels in different food (humus, halawa, tahini, egg plant appetizer in the West Bank.

2. To compare Titanium dioxide levels in food, based on:

    A. type of food

    B. source of food

3. To compare national TiO_2 levels with international levels in order to evaluate the risk of national levels on the general health.

Chapter Two

2. Literature Review

2.1: Sources of Titanium Dioxide

Titanium dioxide is found naturally in various crystal phases. It exists in different crystal structures. anatase, rutile and brookite, or a mixture of these (Warheit et al., 2007). Rutile is the most stable form of TiO_2. Anatase and brookite are stable at normal temperatures but slowly convert to rutile upon heating to temperatures above 550 and 750 °C; respectively (Tang et al., 1994). The stability of TiO_2depends on this crystal structure, the size and shape of the particles (Dudefoi et al., 2017). Main TiO_2 resources are located in Brazil, China, Canada and Australia (Disdier, 2016).

2.2. Production and Use of Titanium Dioxide

The global production of TiO_2 increases with a growth rate of 10% annually, with the beginning of the 1980s, the great acceleration in Titanium production began (Jovanović, 2015) (Annex 3). The amount of Titanium dioxide production in China and the United States ranges between 35% - 45%, each contributing more than 35% of the global market (Jovanović, 2015). For Titanium dioxide nanoparticles (TiO_2-NPs) in Europe, production of 11–1000 tons were reported (Piccinno et al., 2012) and worldwide median produce between 550-5500 ton/ year with range about 3000 ton /year (Jovanović, 2015) Annex 4. The world production in 2014 exceeded 9 million metric tons (El Goresy et al., 2001). Titanium dioxide pigment is produced by either the sulfate process or the chloride Process (Skocaj et al., 2011b). Because of significant environmental and cost issues associated with the sulfate process, most new manufacturing capacity is based on the chloride process (Zhang et al., 2011).

Titanium dioxide has a wide range of applications from paint to sunscreen to food coloring and food supplements or food additive to make good texture and whitening (Oomen et al., 2011).It is one of the most popular pigments used today (Rompelberg et al., 2016) that is used in paints, paper, toothpaste, and plastics, coatings, pharmaceuticals, and cosmetics (Shi et al., 2013, Jovanović, 2015). When used as a pigment, it is called Titanium White, Pigment White 6 (PW6), or CI 77891 (Weir et al., 2012). It is used also as a digestion marker, by using TiO_2as an alternative to chromic dioxide (Cr_2O_3) to facilitate digestibility (Titgemeyer et al., 2001). It is also used in cement, in gemstones, as an optical pacifier in paper (Smook, 2002), and a strengthening agent in graphite composite fishing rods and golf clubs (McCracken, 1999).

Titanium has low price of row material and process so that increase used in food additives which making it more consumed by millions of consumers daily (Skocaj et al., 2011b). It is used in salad dressings, chocolate milk, bakery fillings, cheese, ice cream, sauce and sesame food (tahini, and halawa). When used as a food coloring, it has E number E171 as authorized in the European Union (EU), (Cummins and Hannon, 2017, Commission, 2011). It is commonly used with the crystal structures anatase and rutile as a white pigment in a variety of food items, including chewing gums, candies, chocolate and sweets, largely consumed by children (Weir et al., 2012);(Peters et al., 2014).

Many applications TiO_2NPs are considered in food, water treatments and medical fields (Disdier, 2016). Because of their small size and their high activated surface, interactions with living constituents are facilitated (a NP is 100 000 times smaller than a human cell) (Fabian et al., 2008). TiO_2NPs therefore become issues in toxicology (Xie et al., 2011). The most important point in TiO_2NPs risk assessment is to gain knowledge about the factors and properties which promoting their toxicity the dose tested, exposure time, administration route, biological target and physical characteristics such as size, distribution, aggregation and agglomeration (Disdier, 2016).

2.3. Exposure Routes of TiO_2

Food, cosmetics, and paints have the most common fine particles of TiO_2 effect in human and environment (Robertson et al., 2010). Different physicochemical properties of Titanium dioxide nano particles (TiO_2NPs) lead to different routes enters and toxicity on human and environment health (Farré et al., 2009). The major routes of TiO_{2}-NP exposure that have toxicological relevance in the human are inhalation, dermal, and oral exposure (Shi et al., 2013).

2.4.Inhalation Exposure

Inhalation is one of the major routes for TiO2NPs to gain entry into the human body especially in work place manufacture and processing. The limit for fine particles FPs in the air is 50 µg/m3 for an average human of 70 kg (Simkó and Mattsson, 2010). Some studies suggest that TiO2NPs can translocate from the lung into the circulatory system to systemic tissue and from the nasal cavity into sensory nerves to the nervous system in rat (Wang et al., 2008). In human body, when TiO2NPs are translocate into the blood, generally they may be retained in the liver and lymphatic system, distributed to other organs and tissues, or eliminated out of the body (Halappanavar et al., 2011). The international agency for research on cancer (IARC) had listed Titanium dioxide as "possibly carcinogenic to humans (2B) (Heringa et al., 2016) as inadequate evidence in humans for the carcinogenicity of Titanium dioxide. One of the studies reviewed by IARC had shown a potential risk for occupational workers inhaling Titanium dioxide particles and lung cancer (Boffetta et al., 2001).

2.5. Dermal Exposure

Dermal absorption of TiO_2NPs through several consumer products, such as cosmetics and sunscreens, may contain TiO_2NPs. The outer skin of human beings consists of a tough layer of stratum corneum (SC) that is difficult for inorganic particles to penetrate. TiO_2 particles do not penetrate viable skin, even when the particle size is less than 100 nm and the SC is damaged. Cosmetics and sunscreens containing TiO_2 are normally used on intact skin which is used as pigments more than 70% with fine particles < 100 nm (Nohynek et al., 2007).

2.6. Oral Exposure

TiO_2NPs are also widely used for toothpaste, food colorants, medical capsules and nutritional supplements. Therefore, oral exposure may occur during use of such products. A recent study found that candies such as sweets, chocolate and chewing gums, contained the highest amount of fine particles TiO_2 (Weir et al., 2012). TiO_2 can have toxic effect when utilized as E171 in food manufacture especially at higher age due to accumulation in liver, spleen, and ovaries and can lead to alteration in thyroid function , testosterone level, and increase inflammation level and liver damage (Iavicoli et al., 2012, Iavicoli et al., 2011, Shi et al., 2013, Geraets et al., 2014). The IARC has classified TiO_2 as a Group 2B carcinogen as research suggests consumption that might be linked to oxidative stress, mitochondria damage, neurodegenerative diseases, diseases like Crohn’s, and possibly pose risks for pregnant women. Due to this, the use of Titanium dioxide was re -evaluate in many countries (Additives and Food, 2016).

2.7. Titanium Dioxide in Food

Food and Drug Agency (FDA) is responsible for regulating all color additives to ensure that foods containing color additives are safe to eat and contain only approved ingredients and are accurately labeled, International

Federation of Infection Control, (IFIC) (Council, 2012, Scotter, 2011). The anatase form has been accepted as food pigment much longer than the rutile form (Rompelberg et al., 2016, Warheit et al., 2007). The US FDA has approved the use of TiO_2 in food in 1966 by allowing levels up to 1% in food (Rompelberg et al., 2016). In anatase form, TiO_2 has been accepted as a food additive in the EU for decades as well at quantum satis (i.e. as much as necessary) for a selected list of products (Food additives database) (Rompelberg et al., 2016) and rutile TiO_2has been allowed since 2004, (EFSA, 2004a EU, 2009) .

The white color of pigment TiO_2 is best achieved with particles of 200–300 nm, as these give an optimal diffraction of light for this color (Peters et al., 2014). However, The Titanium Dioxide Manufacturers Association (TDMA) indicated that that the pigment possibly contains particles <100 nm (i.e. nanoparticles (NPs) (Heringa et al., 2016); (Rompelberg et al., 2016); (TDMA, 2013). and the presence of TiO_2 in E171 and in several food products containing E171 such as chewing gum, colored hard-shell candy and icing has been reported (Peters et al., 2014); (Weir et al., 2012);. It is clear that E171 contains NPs and these are present in a series of food products that together may result in a considerable intake of TiO_2NPs (Rompelberg et al., 2016) .

2.8. Human Dietary Intake

Titanium dioxide intake by food, food supplement and toothpaste was measured through food as food additives and toothpaste processing

(Rompelberg et al., 2016) . Several studies have addressed the effects of TiO_2 after oral exposure and significant tissue accumulation over time following repeated exposure due to slow tissue elimination (Reviews by (Iavicoli et al., 2012, Iavicoli et al., 2011). Based on the weight of evidence, a recent risk assessment of dietary exposure to Titanium dioxide NPs via E171 found that risks cannot be excluded for adverse effects in liver, ovaries and testes and therefore the IARC has classified TiO_2 as a Group 2B carcinogen (possibly carcinogenic to humans).

European Food Safety Authority (EFSA), EFSA panel considered that the margins of safety (MoS) calculated from the no observed adverse effects levels NOAEL of 2,250 mg TiO_2/kg body weight per day identified in the toxicological data available and exposure data obtained from the reported use/analytical levels of TiO_2 (E171) would not be of concern(Additives and Food, 2016). Several studies indicate that TiO_2 found in food children higher than others, due to utilized TiO_2 in food colorants such as marshmallow, sweets, halawa ,cake pops (various flavors), chocolate , candies, mayonnaise, whipped cream, yogurts (Skocaj et al., 2011b, Weir et al., 2012). Arizona state university research team put together an estimation of total dietary intake by age and they found that intake may differ greatly between individuals as there are some food groups with an extreme TiO_2 content . The intake TiO_2 as E171 in children under the age of the ten years is estimated being twice that of adults, and the estimated total intake of TiO_2 (as stated by EFSA) is 1.28mg/kg/person (Weir et al., 2012).

2.9. Sources of Titanium Dioxide in the Environment

Sources of TiO_2 in environment present in the two forms, naturally and anthropogenic sources. The most important function of Titanium dioxide is as a pigment for providing brightness, whiteness and opacity to products such as paints, cosmetic, toothpaste, food additives and preservatives (Shukla et al., 2011). The non-pigmentary applications utilize semiconducting and dielectric properties, high stability of TiO_2 such as photovoltaic application in solar cells, photo catalyst applications for oxidizing pollutants, gas sensors (Ni et al., 2007).

Large variety of TiO_2 will be encountered much more frequently due to a high increasing growth in their applications in different products (Robichaud et al., 2009); (Gao et al., 2013) . These applications include cosmetics, skin-care products, paper, sporting facilities, paints, textiles, water purification and soil remediation materials, electronics, and more recently in agriculture and the food industry. The exposure of the human, animals, and plants (e.g., workers and consumers) as well as their release into the environment is expected. Recent studies showed that the TiO_2 demonstrated their capabilities to cause harmful effects on humans and the environment by air pollution, water contamination, and agri-food contamination with TiO_2 (Farré et al., 2009); (Kiser et al., 2012) ; (Lin et al., 2012); (Shi et al., 2013) Annex 5.Therefore, understanding the safety, environmental impacts, and human health implications is very important.

2.9.1. Titanium Dioxide in Air

The main sources of contamination of the general environment with Titanium are the combustion of fossil fuels and the incineration of Titanium-containing wastes and aerosol particles emitted from processed plants and rocks, which goes to air directly (Organization, 1982a). Titanium concentrations in urban air are mainly below 0.1 $\mu g/m^3$ and are still lower in rural air (Organization, 1982a). Concentrations exceeding 1.0 $\mu g/m^3$ have occasionally been reported in urban air and especially in industrialized areas (Rhodes et al., 1972) (Japan Environmental Sanitation Centre, 1967; National Air Pollution Control Administration, 1969 ; US Environmental Protection Agency, 1973). Most of the surfaces and items that are white in color contain TiO_2 (Ahonen, 2001). Thus, TiO_2 containing materials in our homes, workplaces and public areas surround us.

Workplace is defined as a particular environment in which workers are exposed to NPs with the high likelihood of adverse health effects (Luo et al., 2014). The yearly averaged estimated exposure to TiO_2 dust in EU factories varied from 0.1 to 1.0 mg/m^3, and the average levels ranged up to 5 mg/m^3 for individual job categories (Boffetta et al., 2004). The limit for fine particles of Titanium dioxide in the air is 50 $\mu g/m^3$ for an average human of 70 kg (Simkó and Mattsson, 2010, Lee et al., 2011). Concentrations within a range of 0.005–0.021 mg/m^3 in different manufacturing workplaces in EW were measured (van Broekhuizen et al., 2012). Some countries in EU measured TiO_2 with particles/cm^3 because its high surface area (Marra et al., 2010). The American Conference of Governmental Industrial Hygienists (ACGIH) has assigned TiO_2fine particles (FP_S) (total dust) a threshold limit value (TLV) of 10 mg/m^3 as a time weighted average (TWA) for a normal 8 h workday and a 40 h workweek (ACGIH., 2001). permissible exposure limit (PEL) - TWA of the Occupational Safety & Health Administration (OSHA) for TiO_2FPs is 15 mg/m^3 (Kitchin, 2010). Fine particles TiO_2 are transported from the airway rats to the interstitial tissue and subsequently released into the systemic circulation (Mühlfeld et al., 2007).

2.9.2. Titanium Dioxide in Water

TiO_2 in water present in both forms, dissolved or non dissolves particles (Duarte et al., 2014). TiO_2 are being transported to receiving waters with increasing frequency from fertilizer or drug (Luo et al., 2011). Nano-TiO_2 is also considered as an additive of drinking water in water treatment plants in a protocol for the removal of arsenic from water (Höll, 2010). The anthropogenic activities increased the TiO_2 content with hazardous chemicals into urban water systems, such as (Jovanović, 2015):

- Contaminants of emerging concern (CECs), such as diagnostic agents pharmaceutical compounds (PhCs), disinfectants, steroids and phthalates.

- Endocrine disrupting compounds (EDCs), like natural and synthetic estrogenic or androgenic chemicals and fertilizer.

- Personal care products (PCPs), such as cosmetics, fragrances, sun-screen agents (Theissmann et al., 2014).

TiO_2 concentration of surface water from UK averaged 2.1 μg/L in a range of 0.55–6.48 μg/L(Neal et al., 2011). In wastewater treatment plants in USA, the TiO_2 concentration ranged <5.0–15.0 μg/L in the effluents and 1.8– 6.4 g/kg in the biosolids (Annex 5). Similarly, the TiO_2 concentration was about 3.2 μg/L with 305 mg/kg dry weight in biosolids in an activated sludge plant serving over

200 000 people in the UK. It is also reported that effluent Titanium concentrations of less than 25 μg/L in 10 representative WWTPs (Westerhoff et al., 2011).It was found that the total Ti concentrations were 1.6 and 1.8 μg/L in wastewater effluents and 317.4 mg/kg in sewage sludge from Canada (Khosravi et al., 2012). Some algae are able to accumulate Titanium up to 10 000 times and possess the potential to introduce large quantities into the food chain which help to translate TiO_2 to fish then transfer to human and birds (Schroeder et al., 1963).

2.9.3. Titanium Dioxide in Soil and Plants

Concentrations of Titanium can potentially occur in food crops in localized areas as a result of soil contamination by: fly ash fallout (Klein and Russell, 1973, Hallsworth and Adams, 1973, Capes et al., 1974) Industrial contamination and use of industrial, household, and sewage residues for the fertilization of vegetable plots (Kutuzova and Dontsova, 2015, Theissmann et al., 2014). A large quantity of TiO_2-NPs could end up in soils as biosolids are often used as agricultural land amendments (fertilizers). Moreover, the TiO_2-NPs concentration was found to be 2.74 g/kg in surface sediment f (Luo et al., 2011). In another study, the mean Titanium dioxide content in the soils ranged from 6 to 12 g/kg with an average value of 8 g/kg and the content in the clay fraction was higher than that in the silt fraction (Hussain and Islam, 1971). More studies are need to measure TiO_2-NPs in the ecosystem due to pollution and contamination with different sources(Luo et al., 2014). Different studies had demonstrated that TiO_2 accumulates in plants' roots and can accelerate the germination rates (Hong et al., 2005, Gao et al., 2008, Qi et al., 2013)so that its effect on human may be low. TiO_2fine particles less than 20 nm (rutile) cab be accumulate in earthworm at 1g/kg body weight, where they induce DNA and mitochondrial damage (Hu et al., 2010).

TiO_2 was considered as anthropogenic pollutant in soil in Wadi Al-Qilt and was considered one of the major elements concentration found in this location. Wadi Al-Qilt catchment from ten location (Ramallah, al-bireh, mukhmas, qalandiah, stone-cut zone, sweanite, ras-al qilt, murashahat, and sultan) (Harb, 2015).

2.9.4. Titanium dioxide in Cosmetics and Pharmaceutical

TiO_2 is found in different medical and cosmetic products. It has become one of the most widely used materials in industry since 1952 (Bunhu et al., 2011, Nohynek and Dufour, 2012). Food Drug

Administration (FDA) approved used of TiO_2 in sunscreen in 1999 at maximum levels 25% w/w (Newman et al., 2009). The majority of studies suggest that TiO_2NPs, neither uncoated nor coated (SiO_2,$Al_2O_3$and SiO_2/Al_2O_3) of different crystalline structures, penetrate normal animal or human skin (Tyner et al., 2011, Lademann et al., 1999).

2.10. Methods Used to Determined TiO2

Food additives as Titanium dioxide (pure E171) is determine using scanning electron microscopy (SEM), asymmetric flow field-flow fractionation with inductively coupled plasma mass spectrometry (AF4-ICPMS), single particle ICPMS (SP-ICPMS) and acid digestion with inductively coupled plasma optical emission spectrometry (ICPOES) (Luo et al., 2014). In several studies were evaluated for their Titanium dioxide content in food in several materials by using acid digestion and inductively coupled plasma optical emission spectrometry, which is used in Palestinian health ministry (PMOH) and Birzeit University. This method more accurate than other methods such as inductively coupled plasma mass spectrometry (ICP-MS) or scanning electron microscopy (SEM), because it's determine levels of TiO_2 with rapid technique, robust to high levels of acid and matrix, and detects Titanium at levels of parts per billion. Inductively coupled plasma optical emission spectrometry excellent possibilities for quantitative high precision analysis of food. In a study created in 2015 in Jordan about Titanium dioxide content in foodstuffs from the Jordanian market: spectrophotometric evaluation of TiO_2

nanoparticles indicate the absence of TiO_2 from tahini, halawa, canned humus, and jameed, which approved legislation of Institution of Standards and Metrology (Sharif et al., 2014). In the other hand, percentage of TiO_2 content in powdered drinks was 0.19% and in chewing gum was 0.91% not exceeding 1% limit by the FDA. According to Jordanian standard and measurement, powdered drinks and gum it is not approved legislation of Institution of Standards and Metrology in Jordan (Sharif et al., 2014).

In another study (Peters et al., 2014), Twenty four food products were investigated for their Titanium dioxide contents in EU. Nineteen products showed amounts of Titanium higher than 0.1 mg Ti/g product. The highest concentration was found in a chewing gum that contained 5.4 mg Ti/g product which translates to 9.0 mg TiO_2/g product. In general chewing gum showed the highest TiO_2 concentrations while bakery products had the lowest concentration (Peters et al., 2014). The amount of TiO_2 in some food in mg/gram food, in powdered donut was estimated to be 2 mg/gram food, salad dressing (7.5 mg/g food), chewing gum (1.51-3.88 mg/ g food), marshmallows (2 mg/g food), creamed horseradish (2.82 mg/g food), teammate (7.82 mg/ g food), cake icing (1.83 mg/g food), and low fat caesar dressing (0.93% mg/g food) Chen *et al*. 2012), (Weir et al., 2012), (Powell et al., 2000).

2.11. TiO_2 Toxicity

Many studies have evaluate the effects of Titanium toxicity and estimate margin of external exposure of TiO_2 from food intake of human population on organ concentration at which effects were found TiO_2 (liver, spleen, testes, ovary) were indicate risk is possible specially on liver on high age, then on spleen , testes and ovaries (Tassinari et al., 2014), according to the Dutch National Food Consumption Survey (DNFCS), the level of Titanium was determined in some products and the effect of TiO_2 on different ages of the population was divided to children of 2-6 years old, youth 7-6 years old, and the elders over 70 years old. The results suggested estimated TiO_2 particles intake of each age group to be as follows:

- 4.2 mg/kg bw/d for children of 2–6 years old,
- 1.6 mg/kg bw/d for ages 7–69 years, and
- 0.74 mg/kg bw/d for humans of 70 years and older.

Children up to 1 years old were assumed to have no intake of TiO_2 and children of 1–2 years old were assumed to have the same intake as those of 2–6 years old (Rompelberg et al., 2016). Young children consumed confectionary (sweets, chocolates products and chewing gums) and barky wares (biscuits) and young people and children consume much more sweets than older people, these products rich with TiO_2 (Bachler et al., 2015) Annex 6.

In their study, (Geraets et al., 2014) had demonstrated that the Titanium dioxide accumulated in the liver, spleen and lung by 50-80% of the dose taken. On another study, reviewed by (Chen et al., 2013), who found that TiO_2NPs under UV radiation may cause modifications in the DNA leading to cell mutation diseases (e.g., cancer).

In USA population, levels of TiO_2 consumption was estimated on a daily basis by (Bachler et al., 2015, Weir et al., 2012) that show the amount of TiO_2 consumed around 0.2- 0.7 mg of TiO_2 per kg of body weight per day (mg/kg bw/d). In addition to food products, food supplement and medicine contain TiO_2 up to 3.6 mg/g (Authority, 2005).

Chapter Three

3. Methodology

3.1. Background

This study focusees on studying the levels of Titanium dioxide in certain traditional food in the West Bank in Palestine in order to evaluate the risk of national levels on the general health and to compare the results with regional and international studies.

3.2. Study Design

A descriptive study was conducted in 2018. All data regarding TiO_2 concentration in humus, halawa, tahini and egg plants appetizer were obtained from the Palestinian Ministry of Health (PMOH) and from Birzeit University (Center for Testing Laboratories). This includes the level of TiO_2 in each sample source, and type. Food samples number (No. = 444) were analyzed for TiO_2 from 2005 to 2017 in the Palestinian Ministry of Health (PMOH) and Birzeit University**.** Halawa (a flake of confection of crushed sesame seeds in a base syrup), tahini (vegan sesame seed paste), humus (a dip of mashed check peas with tahini) but they can be prepared at home with easy and safe specifications. some studies were conducted on the Halawa and Tahini sold in the markets and found that it is added to the whitening materials to appear in the color of oblique white and this materials may stimulate growth to cancer cells or organs damage (warheit et al., 2007). Egg plants appetizer (mutabale), its Vegetables with preservatives and bleached agent (kuzensof, 2006).

3.3. Sample Collection

All samples were examined in Palestine by the Ministry of Health and Birzeit University, and the information was collected from both sources and classified on the Excel program based on source and type.

The Palestinian Ministry of Health (PMOH) and Birzeit University have examined Titanium from 2005 until 2018. Note that Titanium dioxide was one of the materials that has been allowed in foods such as humus and halawa of 150 mg / kg and tahini of 100 mg / kg of food based on the Palestinian Institute for Standards and Measurement since 2006 (Arij, 2013). After 2015, the use of Titanium in the Palestinian products was banned.

PMoH had examined TiO_2 in different random food samples from shops, Palestinian factories, restaurants and hospitals in order to examine levels of TiO_2 in the food. Before 2015, MoH has used to send the food samples to Birzeit University in order to test TiO_2 levels. Palestinian Consumer Protection Association also sends foods samples to Birzeit University lab in order to examine TiO_2 levels. Palestinian Standards and Metrology used to send the samples for examination to the laboratories of Birzeit University in order to control the quality and to make sure that the product conforms to the specifications and instructions in order to issue quality certificates (ISO or PSI or PSM) to factories or manufacturers and associations, in case they meet the necessary conditions. The Ministry of Economy (Consumer Protection) send samples collected by the observers to the laboratories of Birzeit University to ensure that they are free of Titanium dioxide and within the required specifications. The Palestinian Ministry of Health sent the samples for examination to ensure that the source complied with the mandatory technical instructions to the laboratories of Birzeit University until 2015, When the Ministry of Health decided to examine the samples in its own laboratories. The examination of Titanium material using inductively coupled plasma optical emission spectrometry (ICP- OAS).

3.4. Materials and Methods

The method used to analyze TiO_2 in The Palestinian Ministry of Health (PMOH) and in Birzeit University (Center for Testing Laboratories) was as the following:

3.5. Instrumentation

All analysis were carried out using ~~a~~ inductivity coupled plasma optical emission spectrometry (PerkinElmer, model optima 7300pv) ; (PerkinElmer, optima 3000) and (PerkinElmer, model Avio 200), Data related to TiO_2 concentrates in humus, halawa, tahini and egg plants appetizer in Palestine ministry of health (PMOH) and Birzeit University (Center for Testing Laboratories) in the West Bank from year 2005 to 2017.

3.6. Equipment

- Analytical balance (± 0.0001 g)

- Centrifuge (3500 rpm)
- Hot plate with agitator
- Automatic pipette 1-5ml,100-100µL,20-200 µL
- Thermometer (0-300°$_C$)
- Volumetric Flask 100 ml, 200 ml, 500ml and 1000ml
- Beaker 250 ml
- High speed Blender

3.7. Chemicals and Reagents

All used chemicals were of analytical grade. Concentrated sulfuric acid (98%) and (10 %) were made up in 1.8 mol 1/10, and polypropylene, distilled water or pure water , samples food by inductivity coupled plasma optical emission spectrometry (ICPOE).

3.8. Sample Preparation

All analyses were carried out using an inductivity coupled plasma optical emission spectrometry (ICPOES) but with different models referring to the sources which examined the sample. In (PMOH) using ICPOES instrument with (Perkin Elmer, Model Optima 7300pv) through the following steps **:**

1- Weight 5 grams of the food sample (weight depends on the food type).

2- 10 ml of concentrated sulfuric acid Adding to the sample in a borosilicate glass tube and heated up to 250º c with digested for 1 hour.

3- Samples were cooled at the room temperature.

4- Transferred cooled sample into 50 ml polypropylene centrifuge tube and the borosilicate glass tube was thoroughly rinsed with 10% sulfuric acid and rinsing was added to the polypropylene tube.

5- If precipitate formed, the sample was either centrifuged at 3000 rpm for 5 min and the resulting supernatant fraction was analyzed by ICPOES.

6- A blank samples, using 10 ml of concentrated sulfuric acid without sample, was similarly prepared for every 10 samples.

7- The digested sample volume was made up to 40 ml with 10% sulfuric acid, giving a final acid concentration of 32.5% .

In (Birzeit University) using ICPOES instrument with (PerkinElmer, Model Avio 200) through the following steps:

1- Weigh 5 gram of the food sample (weight depends on the food type).

2- Burn at 600c until completed.

3- Digest ash with 10% concentration sulfuric acid H_2SO_4.

4- Transfer digested to 50 ml volumetric flask and completed volume with milli Q water.

5- Filtered 10 ml from the volumetric flask (microfiltration 0.45 micrometer nylon syringe filter).

6- Run on ICPOES.

3.9. Statistical Analysis

Statistical Products and Service Solutions (SPSS) (version 21, IBM Corporation) was used for data entry and analyses. Characteristics were described using means, standard deviations, and percentages wherever appropriate. The Pearson Chi-square and Fisher exact test were used to compare the categorical variables. A p-value of less than or equal 0.05 was considered statistically significant.

Chapter Four

4. Results and Discussion

4.1. Results and Discussion

The industrial countries and most developing countries have food safety standards and lists of additives for food products. These specifications are reviewed and evaluated periodically through laboratory tests and experiments on experimental animals to determine the physiological and medicinal effect of these substances as well as their effect on growth, appetite, clinical symptoms, their effect on blood, urine results, and on cells and tissues. Titanium dioxide has a wide range of applications from paint to sunscreen to food coloring and food supplements or food additive to make good texture and whitening (Oomen et al., 2011). The amount of food-grade Titanium dioxide that is used in many countries is small. The FDA has set a limit of 1 percent Titanium dioxide for food w/w (Heringa et al., 2016). Animals that were fed different doses with TiO_2 to evaluate its effect experienced cancer or damage of liver and spleen (Tassinari et al., 2014). Mice that were given doses as low as 50 mg/kg body weight experienced hepatic damage in the form of hepatic cell death, increased levels of reactive oxygen species, and altered antioxidant activity, as well as kidney damage (El-Sharkawy et al., 2010).

Many food factories and food restaurants in Palestine have used TiO_2 in food processing as food additives (E171) to enhance color, texture and to increase shelf life of products (Rydström, 2012). Some food factories and restaurants used TiO_2 in daily basis without knowing the limitation of application, and if it is banned or not. Titanium dioxide in some products is still used especially in popular food such as humus tahini, halawa, and egg plants appetizer. These foods are used in large quantities in daily basis.

The geographical distribution of the tested samples is shown in (Table 1). Out of the 444 food samples tested, 207 samples (46.4%) had shown a concentration of TiO_2 percentage higher the permissible limit according to Palestine regulation at Ministry of Health and Palestine standard institution, the legalized concentration after the year 2015 is (0 mg/kg). Table 1 shows that TiO_2 in industrial areas such as Nablus and Hebron is more prevalent than in other areas of the West Bank. This could be due to the high population and the increase in the number of restaurants and food factories in these areas.

The geographical distribution of food samples based on the presence of TiO_2 indicates that the majority of the samples (90.3%) were originally from the West Bank and only 42 (9.5%) were from Egypt and 1 (0.2%) from Turkey. Most local samples tested were from Nablus (number 143 sample), Ramallah and Albeera (87 sample), Hebron (70 sample), and Tulkarm (45 sample). Out of the 42 samples from Egypt, 26 (61.9%) had TiO_2.

Table 1: Geographical distribution of food samples based on presence of TiO_2.

Region	TiO_2	
	No	Yes
	no. (%)	no. (%)
Jenin	3 (42.9)	4 (57.1)
Tubas	1 (50)	1 (50)
Qalqilia	1 (33.3)	2 (66.7)
Tulkarm	24 (53.3)	21 (46.7)
Nablus	79 (55.2)	64 (44.8)
Jericho	21 (77.8)	6 (22.2)
Ramallah and Albeera	42 (48.3)	45 (51.7)
Bethlehem	9 (52.9)	8 (47.1)
Hebron	41 (58.6)	29 (41.4)
Egypt	16 (38.1)	26 (61.9)
Turkey	0 (0)	1 (100)
Total (in all governorates)	237 (53.4)	207 (46.4)

TiO_2 is approved by the FDA and the European food safety authority (EFSA) as food additives to a level of up to 1% by weight (Heringa et al., 2016). In order to evaluate the increased levels of TiO_2 in tested samples, TiO_2 concentration was divided into 5 groups start a concentration of 1 mg/kg (Table 2). Around 46.6% of the food samples tested had TiO_2 levels more than or equal to 1mg/kg. In fact, 31.2% of the samples in all governorates have TiO_2 more than 100 mg/kg. A concentration ranged 100-<1000 mg/kg was measured in all locations except Tubas and Qalqilia. The low sample size in these two locations could be a limited factor to measure high concentrations of $TiO_{2.}$ A concentration more than 1000 mg/kg of TiO_2 was measured in all samples from different locations except Jenin, Jericho and Bethlehem. This means that the levels of TiO_2 in the Palestinian food represent a health risk and all governorates in the West Bank in Palestine are under this risk. Since these types of food are consumed daily in large quantities and by all age groups, this is could be that the harm caused by the food with high TiO_2 distribution encompasses the entire demographic composition of all age groups also. In a neighbouring country, TiO_2 was evaluated in 25 traditional foodstuffs in traditional food in Jordan. Result showed that different proportions in some foods in different locations and they are consumed in very large amounts in Jordan on a daily basis. These foods are tahini, halawa, canned humus, jameed, chewing gum, powder drink. The results showed the absence of TiO_2 in tahini, halawa, humus and jameed. Regarding chewing gum and powder drink, they have TiO_2 content, but not exceeding the 1% limit by FDA, and not complying with the Jordan Institution of Standards and Metrology, which banned. (Sharif et al., 2014).

In this study, most of the samples from Egypt (72.1%) had a concentrations of TiO_2 more than 100mg/kg. The Palestinian market depends heavily on imported products, especially from Turkey, Egypt and China, which necessitates increasing the supervision and testing of these products, especially those suspected to contain Titanium dioxide. The results of the tested Egyptian and Turkish products from halawa showed that they contain quantities that do not meet the Palestinian specifications. The International Agency for Research on Cancer (IARC) has classified TiO_2 as a group 2B carcinogen (possibly carcinogenic to humans) (Boffetta et al., 2001). Therefore, the presence of TiO_2 concentrations at this level propose high health risk especially cancer among the Palestinians. the risk of these concentrations does not have to cause cancer, but a lot of research has study the risk of these concentrations on the organs and cells of the body, especially inflammation and liver damage (Heringa et al., 2016). The presence of these high concentrations in the Palestinian and imported products leads to the emergence of these diseases, especially the children who consume by such products, which appear over the years because of the accumulation of Titanium in the liver and kidneys (warheit et al., 2007).

(Table 2) describes the different levels of TiO_2 tested in different governorates in the West Bank. Although Titanium dioxide has been banned as food additives since 2015 by standard and measurement authority and Ministry of Health (MoH), Titanium dioxide in products is still used in all governorates of the West Bank. The concentration measured in different types of food ranged from 0 mg/kg in 53.4% of the samples to 1000-6000 mg/kg in 11% of the tested samples. Most of the samples with the highest concentration were from Nablus, Tulkarm, Ramallh, Albeera and Hebron.

Table 2: Concentration of TiO_2 based on geographical distribution

Region	**TiO_2 concentrations mg/kg**					
	0	**1-<10**	**10-<100**	**100-<500**	**500-<1000**	**1000-<6000**
	no. (%)	**no. (%)**	**no. (%)**	**no. (%)**	**no. (%)**	**no. (%)**
Jenin	**3 (42.9)**	**0 (0)**	**2 (28.6)**	**2 (28.6)**	**0 (0)**	**0 (0)**
Tubas	**1 (50)**	**1 (50)**	**1 (50)**	**0 (0)**	**0 (0)**	**1 (50)**
Qalqilia	**1 (33.3)**	**0 (0)**	**0 (0)**	**0 (0)**	**0 (0)**	**2 (66.7)**
Tulkarm	**24 (53.3)**	**3 (6.7)**	**2 (4.4)**	**5 (11.1)**	**4 (8.9)**	**7 (15.6)**
Nablus	**79 (55.2)**	**4 (2.8)**	**19(13.3)**	**19 (13.3)**	**8 (5.6)**	**14 (9.8)**
Jericho	**21 (77.8)**	**0 (0)**	**2 (7.4)**	**2 (7.4)**	**2 (7.4)**	**0 (0)**
Ramallah and Albeera	**42 (48.3)**	**4 (4.6)**	**11(12.6)**	**11 (12.6)**	**8 (9.2)**	**11(12.6)**
Bethlehem	**9 (52.9)**	**0 (0)**	**6 (35.3)**	**1 (5.9)**	**0 (0)**	**0 (0)**
Hebron	**41 (58.6)**	**4 (5.7)**	**3 (4.3)**	**10 (14.3)**	**3 (4.3)**	**9 (12.9)**
Egypt	**16 (38.1)**	**2 (4.8)**	**5 (11.9)**	**8 (19)**	**7 (16.7)**	**4 (9.5)**
Turkey	**0 (0)**	**1 (100)**	**0 (0)**	**0 (0)**	**0 (0)**	**0 (0)**
Total (according to each concentrations)	**237(53.4)**	**18(4.1)**	**50(11.3)**	**58 (13.1)**	**32 (7.2)**	**49 (11)**

Hummus, tahini, and halawa are consumed in the West Bank in large quantities in daily base. Therefore, the MoH has focused in measuring of TiO_2 concentration in these food since 2005. The results of the presence of TiO_2 in different types of food are described in (Figure 1). Regardless the concentration, the results indicated that all tested types of food had high concentrations of TiO_2. In all types, halawa significantly was the most frequent type of food that had TiO_2 (47.3%) followed by Tahini (27.1%) and Hummus (23.2%), and finally eggplants appetizer (2.4%) (p value 0.032) (Table 4). All samples that have high TiO_2 from Egypt were halawa. The only sample from Turkey and with TiO_2 was also halawa. Therefore, more monitoring of local and imported halawa is needed.

The use of Titanium dioxide has a major role in the occurrence of health problems, especially cancer, and therefore, the private sectors responsible for food control should increase control and awareness to prevent its use in our products, in addition to preventing the import of such materials. The Central Bureau of Statistics (CBS) 2012 had estimated long term intake and lifelong daily intake of TiO_2 from different food contain TiO_2. It appears many manufactured type of food contain TiO_2 like candies, gum, and baked goods contain TiO_2 0.01 to 1 mg per serving (Rompelberg et al., 2016). The products with the highest Titanium contents are sweets or candies (weir et al, 2012). For example, powdered donuts can contain up to 100 mg per serving (Weir et al., 2012). Types of food are consumed in large quantities by children this may increase the likelihood of liver aggregation or accumulation (weir et al,. 2012: Hong et al,. 2016).

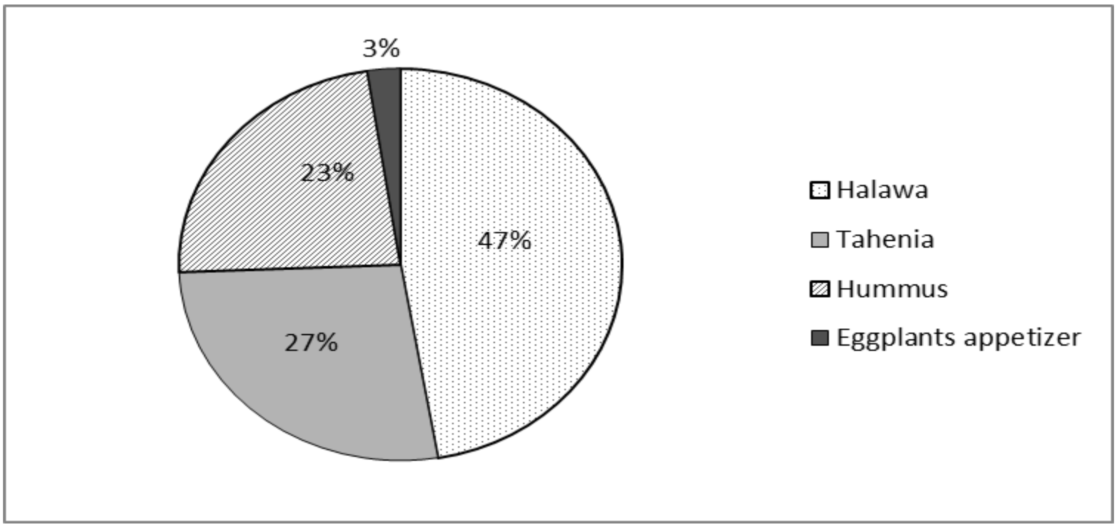

Figure 1: Distribution of food with TiO_2 based on its type. Based on the type of food.

TiO_2 was found mainly in halawa (47.3%) followed by Tahini (27.1%), hummus (23.1%), and lastly eggplant appetizer (2.4%) P value 0.032*.

This could be due to the fact that TiO_2 is added to halawa for whitening and it is found in tahini that is used in preparing halawa. Tahini is added also to hummus but in less quantity.

In order to test if the concentrations of TiO_2 vary in the same type of food depending on its source, we had analysed the concentration of TiO_2 based on the type of food and its source Table (3).

TiO_2 was measured in four types of food, hummus, halawa, tahini, and eggplants appetizer from different sources; restaurants, factories, companies, non-governmental organizations (NGOs), hospitals, and governmental organizations.

Women's associations operate within small projects supported by international organizations (NGO_S) to raise their standard of living. For companies, they are the main source of imported products. The samples sources were as the following: Restaurant (63.5%) for hummus, organizations (84.7%) for halawa, companies (54.9%) for tahini, and factories for egg plants. The results showed that all food prepared manually from restaurants and small woman project have the highest TiO_2 contents. This requires increased control of home-made foods and restaurants and increased awareness of the use of food additives.

Table 3: Source of the different types of tested food.

	Source of the food samples						
	Restaurants	**Factory**	**Company**	**NGOs**	**Hospitals**	**GOs**	**Total**
Hummus	**66(63.5)**	**13(11.9)**	**19(18.6)**	**1(1.2)**	**1(3.7)**	**0(0)**	**100(22.5)**
Halawa	**26(25)**	**37(33.9)**	**20(19.6)**	**72(84.7)**	**20(74.1)**	**8(47.1)**	**183(41.2)**
Eggplants appetizer	**0(0)**	**4(3.7)**	**7(6.9)**	**0(0)**	**0(0)**	**0(0)**	**11(2.5)**
Tahini	**12(11.5)**	**55(50.5)**	**56(54.9)**	**12(14.1)**	**6(22.2)**	**9(52.9)**	**150(33.8)**
Total	**104 (100)**	**109(100)**	**102(100)**	**85(100)**	**27(100)**	**17(100)**	**444(100)**

TiO_2 was found indifferent types of food form different sources (Figure 2). For hummus, samples with TiO_2 were from the following sources, 40.9%, from restaurants, 23.4% of factory samples and 19.6% from companies. Surprisingly, 90% of the halawa made by non-governmental organizations had TiO_2 and 76.9% of the hospital samples had also TiO_2. Most of tahini samples from companies (52.2%) had also TiO_2 (Figure 2). Hummus and halawa are the most consumed products by the Palestinian consumers on a daily basis. Hummus is the main meal of the Palestinian individual as in most Arab countries (ARIJ, 2013).

The small projects implemented by international organizations supporting women's associations are a major source of food in Palestine. In addition, they manage more than 50% of the school canteens in the West Bank (ministry of education,. 2018). Therefore, the use of Titanium in their products constitutes a risk to the largest percentage in the Palestinian society schools.

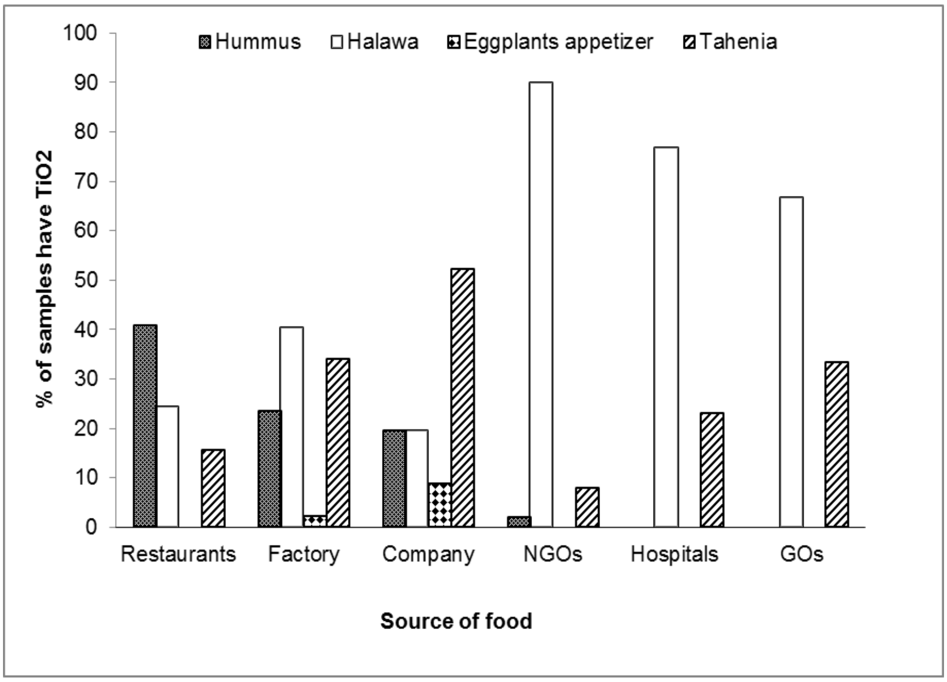

Figure 2: percentage of samples with TiO_2 based on the source.

Based on the source, most of the tested halawa samples from Non-governmental organizations, NGOs, (90%), hospitals (76.9%), and from governmental organizations, GOs. (66.7%) had TiO_2. Most of the tested hummus from restaurants (63.5%) and factories (11.9 %) had TiO_2. Most of the tested food from companies (54.9%) and factories (50.5%) had TiO_2.

Regardless the source, Titanium dioxide was found in different concentrations in all types of food and the concentrations ranged from 2-5400 mg/kg. 53.6% of the tested halawa samples had TiO_2, 72.5% of them had a concentration of TiO_2 more than 100 mg/kg, and 26.5 % of them with a concentration of TiO_2 more than 1000mg/kg. Around 70.8% of hummus samples had TiO_2 in a concentration more than 100 mg/kg, and 29.2% with a concentration more than 1000mg/kg. Around 55.3% of tahini samples had TiO_2 more than 100mg/kg, and 12.5% with a concentration more than 1000 mg/kg (Table 4). World widely, most of the food manufactured are governed by standard specifications and laws that regulate their use and do not permit their circulation except after extensive scientific and technical studies, within safe limits and under the supervision of international organizations with high expertise such as the World Health Organization (WHO) and the Food and Agriculture Organization of the United Nations (FAO). As well as the US Food and Drug Administration and the Scientific Committee on Food for the European Union. FDA identified the use TiO_2 to less than 1% by weight. In Palestine Titanium dioxide was one of the materials that had been allowed in foods such as humus and halawa of 150 mg / kg and tahini of 100 mg / kg of food based on Palestinian Institute for Standard and

Measurement since 2006 (ARIJ, 2013). After 2015, the use of Titanium in the Palestinian product was banded. Therefore, we divided the concentration in the tested food to very low 1- <10 mg/kg, low 10- <100 mg/kg, high 100- <500 mg/kg, very high 500- <1000 mg/kg, and extremely high 1000-6000 mg/kg (Table 4). The results showed the presence of TiO_2 in more than 46.4% of the tested food samples, and ranged from 2- 5400 mg/kg. Its exceeding the 1% limit by the FDA and compromising the presence of TiO_2 in the food, making them unsafe to be consumed. In fact, all tested types of food have very high to extremely high concentrations of TiO_2. These concentrations are considered to be cause of disease (inflammation or cancer) compared to the amount used in animal studies to investigate TiO_2 health effects (Tassinari et al., 2014; Romperberg et al., 2016).

The results of the analysis of the samples of humus containing TiO_2 in the Gaza Strip in Palestine were carried out by the Consumer Protection Ministry of the Palestinian economy in a number of restaurants in 2012, where the results showed the use of Titanium at the rate of 500 to 3000 mg/kg (ARIJ,. 2013).

In order to evaluate the concentration of TiO2 in different types of food, tested food with TiO2 had been divided to different concentrations starting from the lowest 1-<10 mg/kg to the highest (1000-6000 mg/kg). All tested types of food contain very high to extremely high concentrations.

Table 4: Distribution of TiO_2 concentrations in different food types

Type of Food	TiO_2 concentration				
	Very low 1-<10	Low 10-<100	High 100-<500	Very high 500-<1000	Extremely high 1000-<6000
	no. (%)	no. (%)	no. (%)	no. (%)	no. (%)
Hummus	4 (4)	10 (10)	13 (13)	7 (7)	14 (14)
Halawa	9 (4.9)	18 (9.8)	28 (15.3)	17 (9.3)	26 (14.2)
Eggplants appetizer	1 (9.1)	1 (9.1)	0 (0)	1 (9.1)	2 (18.2)
Tahini	4 (2.7)	21 (14)	17 (11.3)	7 (4.7)	7 (4.7)
P value	0.142				

After the year 2015, TiO_2 should be banned and not detected in all samples. However, it was detected in all tested food samples (Table 5). Although there was significant decrease in detecting it in the halawa sample it is still found in 32.1% of the tested samples. In fact, 39.7% of the tested food samples after the year 2015 had TiO_2 in it.

The presence of TiO_2 in many different foods, locally and internationally, contributes to the consumption of TiO_2 more than expected by the Palestinian consumer, because of the consumption of quantities of processed foods not mentioned in this research, such as cake, chewing gum and children's food, which increase the risk of food additives.

Table 5: TiO_2detection in food samples after and before the year 2015

	Before 2015	After 2015	P value
Hummus	3(75)	45(46.9)	0.348
Halawa	80(63.0)	18(32.1)	0.000***
Eggplants appetizer	NA	5(45.5)	NA
Tahini	4(36.4)	52(37.4)	0.999
Total	87(61.3)	120(39.7)	0.000***

Based on the 100 mg/kg that was allowed in tahini and 150 mg/kg in hummus and halawa before the year 2015, 21.6% of the tahini samples had TiO_2 more than 100 mg/kg after the year 2015 and 28.1% and 23.3% of the hummus and halawa respectively had concentration of TiO_2 more than 150 mg/kg (Table 6).

Table 6: Difference in TiO_2concentration before and after 2015

Type of Food	TiO_2 concentration	
	Before 2015	After 2015
	no. (%)	no. (%)
Hummus based on >150 mg/kg	2 (50)	27(28.1)
Halawa based on >150 mg/kg	49(38.6)	13(23.2)
Tahini based on> 100 mg/kg	1(9.1)	30(21.6)

The results showed in Table (6) that the use of Titanium after 2015 has increased in humus and tahini, indicating the increase in the use of Titanium in restaurants and factories despite the issuance of a law ban use after 2015, which calls for more effective application of the Palestinian law to protect consumers from the risks of the use of Titanium and its impact on public health. TiO_2 concentration of these products was generally higher than the values for comparable products from literature, these products were chosen as more common by ministry of health. Despite, many of the products contributing may contain similar concentration of TiO_2, and are used in other countries as well depending on habits, for example, dry milk containing TiO_2 or Ti (see annex 7) (Rompelberg et al., 2016). Also in some products, low levels have been observed that may not originate from added TiO_2 (Peters et al., 2014). Based on the data of about 20 products in which both TiO_2 and Ti content were measured (Peters et al., 2014), this is evidence of individual consumption of TiO_2 more than expected results.

Difference in TiO2 concentration levels between location refer to food types, sources, habits and culture. For example, factories have lows and regulations on the use of additives, but restaurants and associations have often used additives without knowing and abiding by them.

Quantitatively, there were significant differences in the levels of Titanium dioxide present in these food products, ranging from 2 - 5400 mg/kg in foods. Other similar products may also contain high levels of Titanium dioxide, mentioned in literature. However, there is no mechanism to indicate the volume of Titanium dioxide added in different food products.

Chapter Five

5. Conclusions and Recommendations

5.1. Conclusions

1. Total number of 444 tested of food sample were analysed for TiO_2 content, these food (humus, tahini, halawa, mutable) were chosen, because they are consumed in very large amount in the West Bank on a daily basis (Palestinian traditional food).

2. TiO_2 in the Palestinian products has different concentration according to type of food and sources (0.0 mg/kg – 5400 mg/kg).

3. The results showed that 46.4% of foods analysis does not complied with Palestine Institution of standards and metrology for locally manufactured items and FDA regulation for exported food.

4. The presence of TiO_2 was high concentration in the most tested food samples, that contain TiO_2, and that can cause cancer or mutation.

5.2. Recommendations

Main recommendation of this research is that more studies are needed to evaluate:

1. Increased interest in the control of local products containing Titanium, especially in Nablus, Tulkarem and Hebron, which is the

most commonly used TiO_2 in processed foods. As well as increased control over imported products contain TiO_2.

2. The need to increase the examination of foods that contain the most TiO_2, especially children's food such as sweets, marshmallow, cake pops, chocolate, mayonnaise, yogurt, juice.

3. The examination of TiO_2 in the Palestinian food periodically and regularly by the competent authorities.

4. Activation of the law banning the use of Titanium in Palestinian processed food after 2015.

5. Raising awareness of NGOs supporting small enterprises and Associations to prevent the use of Titanium in their products.

6. Raising awareness among Palestinian citizens about the disadvantage of additives and preservatives such as TiO_2.

7. Studying the percentage of TiO_2 in the ponds and sources of drinking water in Palestine.

8. Children and older should be offered natural food or free of TiO_2, especially traditional food, sweets, marshmallow, juice, chocolates.

5.3. Limitations

- Do not examine different samples of foods expected to be contained on Titanium dioxide by the Ministry of Health and related institutions.
- The Ministry of Health does not carry out periodic and regular inspections of Titanium dioxide in these foods.

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Annexes

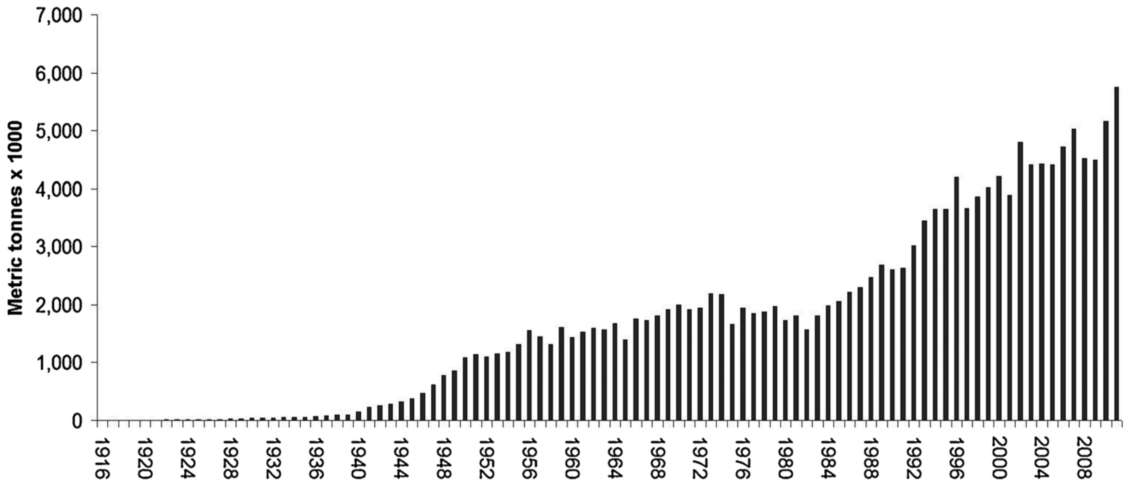
Annex 1: Physical and chemical characteristics of TiO_2(Murray, 2006)

physicals and chemicals characteristics of Titanium dioxide	
Color	white
Colour Index	Pigment White 6 (77891)
Chemical Name	Titanium Dioxide (Rutile)
Chemical Formula	TiO_2
CAS No.	13463-67-7
EINECS No.	236-675-5
Production	Rutile pigment produced by the chloride process
Density	4.1 g/cm^3
Specific Gravity	4.1
Bulk Density	34.2 lbs/gal 119.8 kg/m^3
pH Value (10% suspension)	7.5

Annex 2: Names of TiO_2, regulation process, trade names, IUPAC names (Number and Insert Annex)2016.

EC number:	236-675-5
EC name:	Titanium dioxide
CAS number (EC inventory):	13463-67-7
CAS number:	13463-67-7
CAS name:	Titanium oxide (TiO2)
IUPAC name:	dioxoTitanium
CLP Annex VI Index number:	-
Molecular formula:	TiO_2
Molecular weight range:	79.8

Annex 3: Historical production of Titanium dioxide pigment by all countries of the world combined(USGS., 2013).



Annex 4: Production quantities of TiO_2–NPs in China and the rest of the world

Country /region	Production (ton /year)	Reference
China	1300	Gao *et al.*,2013
Europe median (25/75precentile)	550 (55-3000)	Piccinno *et al.*,2012
USA range	7800-38000	Hendren *et al.*,2011
Switzerland	435	Schmid and Riediker, 2008
Worldwide median (25/75 percentile)	3000 (550-5500)	Piccinno *et al.*,2012

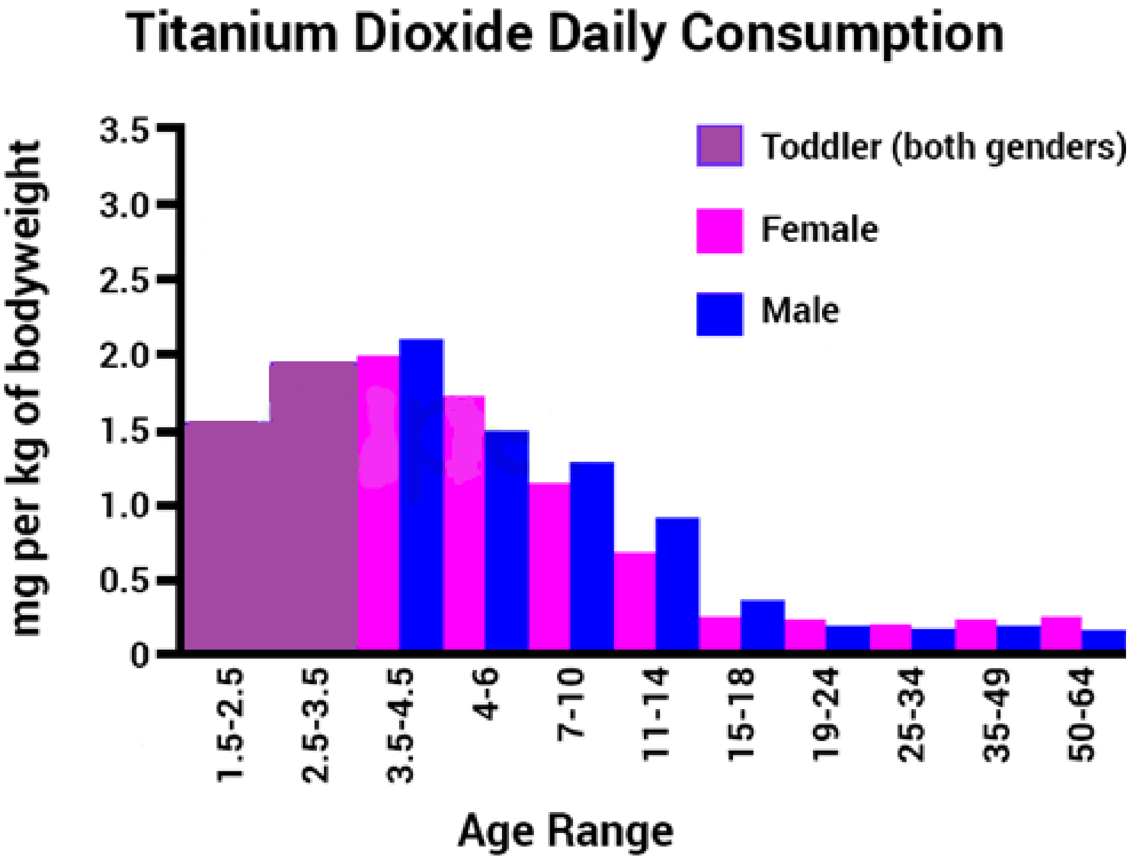
Annex 5: Measured TiO_2-NP in different environmental matrix and various analytical methods (Luo et al., 2014)

Measured environmental TiO_2-NPs in different environmental matrixes and various analytical methods

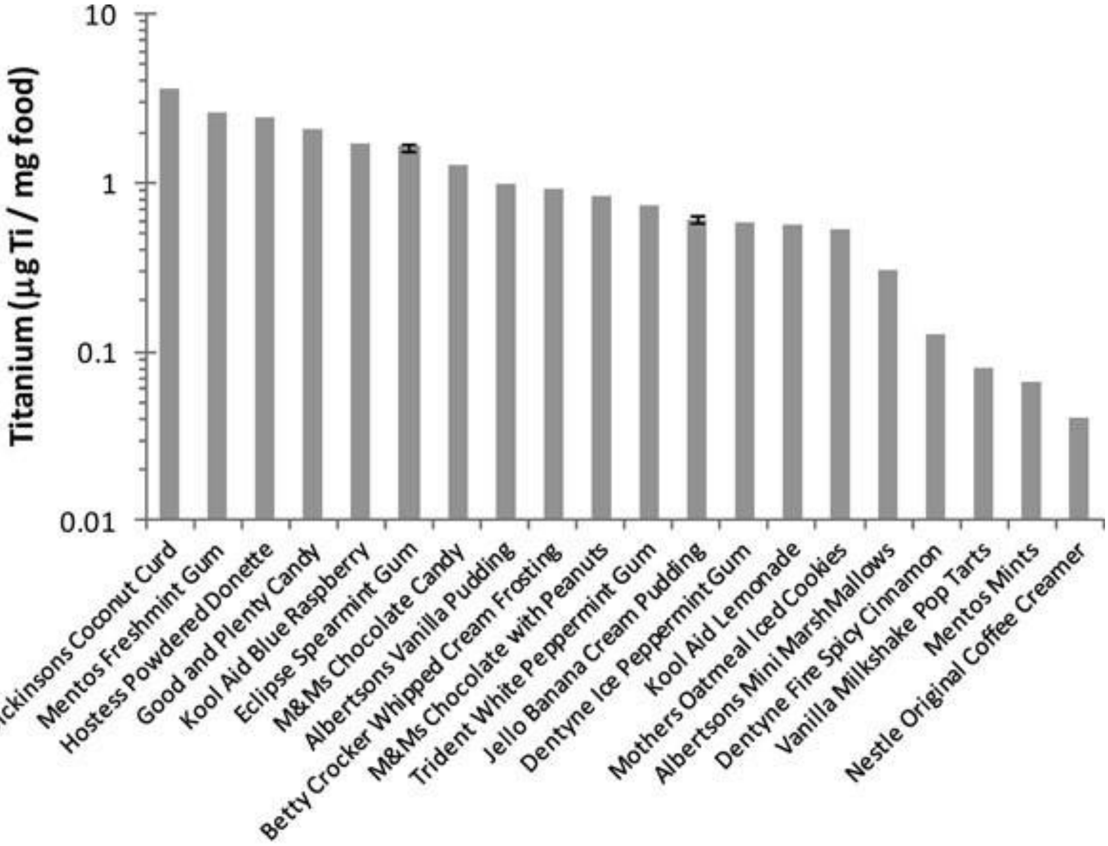
Environmental matrix	Concentration	Measurement method used	Reference
Workplace	11 418–45 889 particles/cm^3 for manufacturing workplace; 9512–16 337 particles/cm^3 for European construction industries	CPC, SMPS, DC	Duarte *et al.*, 2014
Surface water	2.1 (0.55–6.48) μg/L	Filtration, CFU, ICP-MS	Neal *et al.*, 2011
Wastewater treatment plants effluents	<5.0–15.0 μg/L; 3.2 μg/L; <25 μg/L; 1.6 &1.8 μg/L	Filtration, RDL, digestion, ICP-OES, SEM+EDX	Kiser *et al.*, 2009; Johnson *et al.*, 2011; Westerhoff *et al.*, 2011; Khosravi *et al.*, 2012
Biosolids	1.0–6.0 g/kg; 305 mg/kg; 317.4 mg/kg	Filtration, digestion, ICP-MS, SEM+EDX	Kiser *et al.*, 2009; Johnson *et al.*, 2011; Khosravi *et al.*, 2012
Sediment	≤2.74 g/kg	Microwave aid acid digestion, ICP-MS, SEM+TEM+EDX	Luo *et al.*, 2011

CFU: cross flow ultrafiltration; RDL: rota-evaporation, dialysis, and lyophilization

Annex 6: TiO_2 daily consumption (Rompelberg et al., 2016)



Annex 7: The amount of Titanium found in certain popular consumer products. [Weir et al., 2012]



جامعة النجاح الوطنية
كلية الدراسات العليا

تقييم نسبة ثاني أكسيد التيتانيوم الموجود في الطعام في الضفة الغربية

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قدمت هذه الأطروحة استكمالاً لمتطلبات الحصول على درجة الماجستير في العلوم البيئية بكلية الدراسات العليا في جامعة النجاح الوطنية في نابلس، فلسطين.

2018م

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الملخص

على الرغم من حظر ثاني أكيد التيتانيوم (TiO_2) كمادة مضافة إلى الطعام منذ سنة ٢٠١٥ وفقا لمعايير الأمان ونظم القياس الدولية ووزارة الصحة الفلسطينية، لا يزال يستخدم خاصة في الأطعمة المشهورة كالحمص والطحينية والحلاوة. قد يكون ثاني أكسيد التيتانيوم شاغلا صحيا ويجدر بِنَا تقييم مخاطرة. إنّ الهدف من هذا البحث هو تقييم نسبة ثاني أكسيد التيتانيوم في أشهر الأطعمة الفلسطينية وهي الحمص والطحينية والحلاوة بالإضافة إلى مقبلات مصانع البيض في سنوات ٢٠٠٥–٢٠١٧ ولمقارنة مستوياته قبل وبعد أن تم حظره من تلك الأطعمة. لقد تم اختبار ثاني أكسيد التيتانيوم في ٤٤٤ عينة مأخوذة من مختلف أنواع الأطعمة كالحلاوة والحمص والطحينية ومقبلات مصانع البيض منذ سنة ٢٠٠٥ وحتى سنة ٢٠١٧ من قبل وزارة الصحة الفلسطينية (PMOH) وجامعة بيرزيت (مركز معامل الاختبارات). من ضمن العينات التي تم اختبارها، أظهرت ٢٠٧ عينة (٤٦.٤٪) أن تركيز ثاني أكسيد التيتانيوم بشكل أكبر من الحد المسموح به. لقد كانت معظم العينات (٩٠.٣٪) من الضفة الغربية بالأصل بينما كانت ٤٢ من العينات (٩.٥٪) من مصر وعينة واحدة (٠.٢٪) من تركيا. تم اكتشاف وجود ثاني أكسيد التيتانيوم في ٤٦.٦٪ من هذه النماذج و(٦١.٩٪) من العينات المصرية تم العثور على ثاني أكسيد التيتانيوم فيها. تم اكتشاف وجوده في ٦.٥٣٪ من عينات الحلاوة و ٤٨٪ في عينات الحمص و٣.٣٧٪ في عينات الطحينية . لقد وُجد أن جميع العينات المختبرة تحتوي على نسبة عالية من ثاني أكسيد التيتانيوم وتتراوح بين (٢–٥٤٠٠) ملغم/كغم وحتى بعد سنة ٢٠١٥ عندما تم حظره من قبل وزارة الصحة الفلسطينية. تعد المشاريع الصغيرة الممولة من قبل منظمات غير

حكومية بالإضافة إلى المطاعم أكبر مصدر للأطعمة المحتوية على ثاني أكسيد التيتانيوم. تبين نتائج الدراسة أن ثاني أكسيد التيتانيوم في الأطعمة الفلسطينية المشهورة يشكل تهديدا حقيقيا للصحة الحالية والمستقبلية في فلسطين. لذا فإننا نحتاج إلى المزيد من التنظيم والرقابة بالإضافة إلى تقليل الإنفاذ. ويجب القيام بدراسات أخرى عديدة لاكتشاف الخطر الذي يمكن أن يتسبب ثاني أكيد التيتانيوم فيه من أجل إنشاء توجيهات محددة من الاستراتيجيات الوقائية.