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Department of Land, Environment, Agriculture and Forestry

Corso di laurea magistrale/Second Cycle Degree (MSc)

in Food and Health

Aloe and products thereof in the food industry: a regulatory study

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Abstract

This study analyses the food industry's use of aloe and its derivatives. It emphasizes regulatory aspects related to safety, labelling, and quality standards. The study evaluates the regulatory frameworks established by various nations and international organizations, such as the FDA and EFSA, to regulate the use of aloe in food items. The properties and permitted applications of various aloe forms, including gel, extracts, and latex, are analysed. In order to ensure consumer safety, safety assessments, toxicological studies, and potential adverse effects associated with aloe consumption are reviewed. This study investigates the requirements for labelling and claims for aloe-containing food products, including health and nutritional claims. This study concludes with a thorough overview of aloe in the food industry, focusing on safety, labelling, and quality standards. Additionally, the study identifies avenues for additional research and development to promote innovation in aloe-based culinary products while sticking to existing rules and regulations.

CHAPTER I

INTRODUCTION

I.1. General information

The vast majority of *Aloe vera* or 42 species of them, originate from Madagascar. The region known as the Arabia is home to 12–15 species, and India is home to 4 species. The remaining species originate from different tropical countries. About thirty of them, including *Aloe spicata*, *Aloe perryi Baker*, *Aloe socotna*, *Aloe africana Miller*, *Aloe chinensis*, *Aloe perfoliata*, and *Aloe saponaria*, have been examined, and their curative qualities have been verified. However, *Aloe barbadensis*, also known as *Aloe vera*, *Aloe ferox*, also known as bitter aloe, and *Aloe aborescens*, also known as krantz aloe, are the three most prevalent species, and these are the ones that are commonly employed for commercial manufacturing. The effects that different species of aloe have on the human body are not the same. There are some species that have therapeutic properties, while others either have poisonous or neutral effects (Benzie & Wachtel-Galor, 2011).

Aloe barbadensis Miller, also known as *Aloe vera Linne*, is the most popular; it is a perennial plant with a short stem that can reach a height of between 60 and 100 cm. The leaves of aloe plants are often thick, sword-shaped, and green or gray and green in color. Thorns in the shape of triangles can be found along the leaf margins. The bell-shaped pink and orange blooms that make up the flower shoot are produced in abundance during the summer when the plant is actively growing. Bags are the fruit that are produced by the plant after the blossoms have fallen off (Benzie & Wachtel-Galor, 2011). The term "aloe" originates from the Arabic word "alloeh", which translates to "bitter and shiny substance". Similarly, the term "vera" is derived from the Latin word denoting "truth". Its original habitats include the eastern part of Africa, the Arabian Peninsula, the Indian subcontinent, and the Mediterranean region (Grindlay & Reynolds, 1986; Viljoen & Van Wyk, 2000). In addition to India, Cyprus, Malta, Sicily, and the Canary Islands all have a healthy population of *Aloe vera* plants that are found in their natural state (Radha & Laxmipriya, 2014). The island of Barbados and the northern states of the United States are home to some of the world's largest *Aloe vera* plantations. Aloe can have either branching or unbranched stems, and its leaves are covered and greyish green with sharp edges. These leaves create a rosette. The leaves are packed with a milky fluid that might be brown or yellowish in color and contains the majority of the medicinal chemicals (Benzie & Wachtel-Galor, 2011). Aloes are classified as perennial succulents or xerophytes, indicating their ability to thrive in environments with limited or unpredictable water availability. They possess the unique ability to store significant amounts of water in their tissues and employ a photosynthetic pathway known as CAM

(Crassulacean Acid Metabolism) as an adaptation to hot climates. CAM involves the production of malic acid (Ni et al., 2004) (Takahashi et al., 2005). A limited number of Aloe species hold significance in the commercial realm, with *Aloe vera* being widely acknowledged as the most potent and hence enjoying the highest level of popularity (Eshun & Qian, 2004; Ni et al., 2004). *Aloe vera*, a succulent plant resembling a cactus, demonstrates an ability for surviving in desert and warm environments. Presently, due to its high demand, extensive cultivation of this plant is undertaken (Vogler & Ernst, 1999).

Aloe vera, referred to as the "plant of immortality" in ancient Egypt, has been utilized as a conventional form of medicine in various cultures including Arab, Chinese, Egyptian, Greek, Indian, Japanese, Korean, and Roman societies (Grindlay & Reynolds, 1986; Atherton, 1998). For over 2,000 years, it has been empirically employed to address a wide range of disorders and ailments, including but not limited to skin conditions such as wounds, x-ray and radium burns, and psoriasis, as well as constipation, external and internal ulcers, hyperlipidaemia, diabetes, and lupus erythematosus (Reynolds & Dweck, 1999; Atiba et al., 2011; Foster et al., 2011; Vogler & Ernst, 1999). The production of *Aloe vera* has gained prominence as an emerging industry due to its purported beneficial effects. This industry encompasses the manufacturing of laxative drugs, cosmetics, and functional food products. These products include face and hand creams, foundations, cleansers, lipsticks, suntan lotions, shampoos, hair tonics, shaving preparations, bath aids, makeup, fragrance preparations, baby lotions, wipes, yogurt, drinks, capsules, and tablets (Barnes et al., 2008).

The utilization of herbal items has experienced a significant surge in popularity among the general populace. According to the findings of the National Health Interview Survey in 2007, it was observed that almost 40% of the American population, encompassing both adults and children, engaged in the utilization of complementary and alternative medicine as an alternative form of therapy within the preceding 12-month period (Nahin et al., 2009). Approximately $14.8 billion was expended on the acquisition of non-vitamin, no mineral natural products, constituting 44% of the total out-of-pocket expenses for complementary and alternative medicine (Hamman, 2008). *Aloe vera* has a rich historical background in offering a diverse range of health advantages, making it a widely utilized herbal remedy throughout many regions globally (Guo & Mei, 2016).

CHAPTER II

COMPOSITION OF *ALOE VERA* LEAF

II.1. **Structural composition**

Aloe vera is a succulent and delicate plant that has a high percentage (99–99.5%) of water content in its leaves. Solid contents range from 0.5 to 1% and are made up of a wide variety of active components, such as minerals that are both fat and water soluble, vitamins, simple and complex polysaccharides, organic acids, enzymes, and phenolic compounds (Hamman, 2008). The three layers that make up the leaf are the gel, the latex, and the cuticle (Lee et al., 2004). The *A. vera* leaf is composed of three primary parts: the outer, thick green rind with white teeth along the borders; the inner, viscous jelly-like mucilage layer; and the fillet fluid, the plant's water storage region (Chandegara & Varshney, 2013).

• Gel, inner layer composed of soft, transparent, damp, and slick tissues with large parenchyma cells. This substance resembles a transparent mucilaginous gelatin. It is composed of 99% water, glucomannans, amino acids, lipids, sterols, and vitamins (Hamman, 2008; Benítez et al., 2015; Ramachandra & Rao, 2008).

• Latex is the layer in the centre of the plant that contains anthraquinones, yellow sap that is bitter, and glycosides (Hamman, 2008). The mesophyll, below the rind, contains xylem and phloem vascular bundles that transport nutrients and water from the roots to the leaves and store latex in the leaf edges. The mesophyll has the most latex anthraquinones, anthrones, and chromones, as well as coumarins, flavonoids, and pyrones (Baldi et al., 2021).

• Rind the thick outer layer consisting of 15-20 cells that protects the plant from environmental stresses and moisture loss and aids in the synthesis of carbohydrates and proteins (Misir et al., 2014); accounts for 20-30% of the fresh leaf's weight. There is a wax cuticle and a chloroplast-rich region where the plant's photosynthetic pathways occur. The rind is mostly made up of structural components, but it also has trace amounts of oxalic acid, anthraquinones, and derivatives thereof. These substances are well-known to be phytopathogen-resistant (Baldi et al., 2021).

Both the flesh and pulp that can be extracted from *Aloe vera* have distinctive chemical make-ups and physical characteristics. The aloe meat can be obtained by peeling the leaves of the aloe plant, washing them, and then carefully squeezing them. The result of this method is pure flesh that does not have an aftertaste of bitterness or strong laxative qualities. The flesh of an aloe plant is pale green in color and has the viscosity of jelly. It is made up of dry matter (4%), which has protein (6.86%), fat (2.91%), dietary fiber (73.35%), ascorbic acid (0.004%), and ash (16.88%) (Zhang et al., 2018).

The composition of this substance is water (96%) and dry matter (4%). In addition to the flesh, aloe pulp also includes the skin. It has not been washed or filtered, and as a result, it has a high amount of aloin, which gives it powerful laxative qualities (Hęś et al., 2019).

II.2. Chemical composition

Each *A. vera* leaf is composed of two components: an outer green rind and a transparent pulp inside. The pulp constitutes the primary component of the leaf in terms of volume, exhibiting a transparent and gelatinous appearance (Reynolds, 2004).

The core parenchyma tissue of *A. vera* leaves and the exudate from cells near to the vascular bundles contain several chemicals with various structures. The 1,8-dihydroxyanthraquinone glycosides and other compounds found in the bitter yellow exudate are traditionally employed for their cathartic properties (Vázquez et al., 1996). There are many different types of carbohydrates in aloe, but there are also proteins, lipids, amino acids, vitamins, enzymes, inorganic compounds, and tiny organic compounds found in the aloe parenchyma tissue or pulp. Some aloe polysaccharide composition shows chemotaxonomic diversity (Reynolds, 2004; Cosmetic Ingredient Review Expert Panel, 2007; Ni & Tizard, 2004).

When the leaves of most *A. vera* species are incised, a somewhat abundant exudate is released, initially appearing yellow but quickly transitioning to a brown color or, in select species, a dark red hue. The exudates consist of phenolic chemicals that may be differentiated by chromatographic methods. Most of the exudate chemicals that have been identified thus far belong to the categories of chromone, anthraquinone, or anthrone derivatives. Certain compounds exhibit a wide distribution within the genus, while others are limited to only a few species, thereby indicating their potential significance in chemotaxonomy. The presence of phenolics is not observed in the parenchyma cells located within the leaf, which are known for their unique composition of polysaccharides and glycoproteins. The exudate has a significant concentration of aloin, amounting to 28% on a wet basis. Aloin is a C-glucoside of aloeemodin anthrone (Reynolds, 2004).

II.3. Chemical composition of gel

Aloe vera gel is a clear, colorless, and viscous mucilaginous gel made from the parenchymatous cells found in *Aloe vera* leaves. The *Aloe vera* gel mostly consists of water and polysaccharides, including including pectins, hemicelluloses, glucomannan, acemannan, and mannose derivatives.

Moreover, it has been found that aloe gel contains carbohydrates, proteins, lipids, amino acids, sterols, vitamins, tannins, enzymes, metal compounds, and small organic compounds. (Atherton, 1998).

II.4. Chemical composition of the latex leaf lining

Anthraquinone glycosides, namely aloin, aloe-emodin, and barbaloin, are of interest in academic research (Atherton, 1998).

The gel or mucilage derived from the mesophyll tissue of the leaf consists of distinct components in comparison to the bitter latex collected from the leaf's inner lining (Klein & Penneys, 1988). *A. vera* gel, commonly found in several non-prescription skin salves, consists of approximately 99% water and has a pH level of 4.5. The gel is comprised of a polysaccharide known as glucomannan, which functions as an emollient. The product is an effective moisturizer, which explains its widespread application in many cosmetic formulations (Christaki & Florou-Paneri, 2010).

Acemannan, the primary carbohydrate component found in the gel, is a soluble polymer composed of long chains of mannose. It has been observed to enhance the healing process of wounds, regulate immunological function by influencing macrophage activation and cytokine production, and exhibit properties that inhibit the growth of tumors and viruses (Peng et al., 1991). The gel formulation additionally includes bradykininase, an agent with anti-inflammatory properties (Yagi et al., 1982). It also contains magnesium lactate, which serves as an itch-preventing agent. Furthermore, the gel incorporates salicylic acid and other anti-prostaglandin ingredients that effectively alleviate inflammation.

The leaf lining of the plant includes anthraquinone glycosides, namely aloin, aloe-emodin, and barbaloin, which possess strong stimulating laxative properties. The water-soluble glycosides undergo hydrolysis by intestinal bacteria, resulting in the formation of aglycones that contribute to the laxative effect.

II.5. Active components present in *A. vera* and their properties

There are seventy-five potentially active ingredients in *A. vera*, including vitamins, enzymes, minerals, sugars, lignin, saponins, amino acids, and salicylic acids (Foster et al., 2011).

The vitamin composition of *A. vera* comprises vitamins A (beta-carotene), C, and E, all of which work to prevent cancer, can be found in it. Besides that, it has choline, vitamin B12, and folic acid. Antioxidant neutralizes free radicals (Sharma & Pegu, 2019; Surjushe et al., 2008).

With regards to other components, *A. vera* contains eight different enzymes, including aliiase, alkaline phosphatase, amylase, bradykinase, carboxypeptidase, catalase, cellulase, lipase, and peroxidase. When applied topically, bradykinase helps reduce excessive inflammation, while other enzymes aid in the digestion of carbohydrates and lipids (Sharma & Pegu, 2019; Surjushe et al., 2008).

It is rich in minerals like calcium, chromium, copper, selenium, magnesium, manganese, potassium, sodium, and zinc. Few of these are antioxidants, but all are essential for the proper operation of different enzyme systems along different metabolic pathways (Sharma & Pegu, 2019; Surjushe et al., 2008).

Sugars such as glucose and fructose, two monosaccharides, are present in addition to two polysaccharides, glucomannans and polymannose. These are called mucopolysaccharides, and they are extracted from the mucilage of the plant. Monosaccharide mannose-6-phosphate and polysaccharide glucomannans [beta-(1,4)-acetylated mannan] are the most common. There is also acemannan, a well-known glucomannan. The antiallergic glycoprotein alprogen and novel anti-inflammatory compound C-glucosyl chromone were isolated from *A. vera* gel (Ro et al., 2000; Hutter et al., 1996). It contains twelve anthraquinones, which are phenolic substances that have historically been used as laxatives. Aloin and emodin have antiviral, antibacterial, and analgesic properties (Sharma & Pegu 2019; Surjushe et al., 2008). Fatty acids: It contains four different types of plant steroids: cholesterol, campesterol, beta-sitosterol, and lupeol. Each of these has anti-inflammatory qualities, and lupeol also has analgesic and antiseptic qualities (Sharma & Pegu, 2019; Surjushe et al., 2008).

Hormones like Gibberellins and auxins, which have anti-inflammatory and wound-healing properties are present in *A.vera*. (Sharma & Pegu 2019) (Surjushe et al., 2008).

Additionally, seven of the eight essential amino acids are found in it, along with 20 of the 22 amino acids that humans need. Additionally, it has salicylic acid in it, which can reduce inflammation and kill bacteria. Topical preparations with lignin, an inert substance, increase skin penetration. About 3% of the gel is made up of the soapy substances called saponins, which are also antiseptic (Sharma & Pegu, 2019; Surjushe et al., 2008).

II.6. Adverse effects/toxicity of *A. vera*

Following literature study, the EFSA found *A. vera* extracts to be genotoxic in vitro (European Food Safety Authority, 2018). This is probably because of the existence of HADs. It has been shown that 1) aloe-emodin can damage genes in mice; 2) *A. vera* whole leaf extract with HADs can cause cancer in rats; and 3) danthron, a structurally similar compound, can cause cancer in rodents. Additionally, a report on *A. vera* by the International Agency for Research on Cancer (IARC) raises safety issues (International Agency for Research and Cancer, 2015). *A. vera* whole leaf extract was found to be carcinogenic in animal studies, according to the International Agency for Research on Cancer. Because of this, this specific kind of aloe preparation is regarded as having the potential to cause cancer in human beings (Group 2 B). However, the European Food Safety Authority (EFSA) does

not differentiate between the toxicity of different types of Aloe preparation (gel, whole leaf extract, latex) in its opinion, and instead refers to a general "Aloe extract", while the International Agency for Research on Cancer (IARC) only attributes this carcinogenic activity to *A. vera* whole leaf extract (Baldi et al., 2021).

Topical and oral *A. vera* can cause skin irritation, hives, cramping, and diarrhoea in people allergic to onions and tulips. There are no controlled toxicology studies on Aloe products, but there are several case reports on human toxicity or hypersensitivity (Steenkamp & Stewart, 2007). It has been observed that a patient with stasis dermatitis developed widespread dermatitis after using *A. vera* gel. When used topically after dermabrasion, *Aloe vera* gel has caused a burning sensation and dermatitis in few individuals (Hunter & Frumkin, 1991). Because of the risk of contamination by anthraquinones, ingesting *A. vera* gel orally might result in symptoms like stomach cramping and diarrhea. Several studies on both animals and humans have shown that *A. vera* gel can reduce plasma glucose (Ghannam et al., 1986). No in vivo toxicity studies have been reported in humans, however there are some single-case accounts. After using *A. vera* pills, one patient developed significant intraoperative bleeding. Because of a probable interaction between *A. vera* and sevoflurane (Lee et al., 2004), this happened. An individual with acute renal failure due to intake of *A. vera* was described by literature (Luyckx et al., 2002). A further study described a patient who experienced severe vomiting after ingesting *A. vera* (Wu et al., 2003), while some scholars (Willems et al., 2003) reported a case of *melanosis coli* that occurred after the patient self-medicated with anthranoids for an extended period of time. There have been reports of acute hepatitis after consuming *A. vera* (Rabe et al., 2005) and *Henoch-Schonlein purpura* after consuming *A. vera* herbal medicine juice for back pain (Evangelos et al., 2005). Researchers found that there was no evidence of acute toxicity in therapeutic levels when tested on mice; nevertheless, a reduction in central nervous system (CNS) function was observed in high doses (Shah et al.,1989). In prolonged treatment, the number of red blood cells dropped and sperm suffered a lot of damage (Shah et al., 1989). In humans, no systematic study has examined the effects of large *A. vera* dosages for longer durations on red cell count and sperm destruction (Vogler & Ernst, 1999).

The use of *A. vera* as an abortifacient has been linked to fatalities. In any case, *A. vera* toxicity has not been shown as a cause of mortality (Vago, 1969). The LOAEL for aloin is calculated as 11.8 g/kg BW (Zhou et al., 2003), while 2 g/kg BW of *A. vera* whole-leaf powder has been found to have adverse effects. During pregnancy, avoid *A. vera* latex because to its cathartic effects, which may produce strong uterine contractions and raise the chance of miscarriage. Ingesting it may induce severe cramps and diarrhea in infants, thus nursing mothers should avoid it (Brinker, 1998).

CHAPTER III

USES OF *ALOE VERA*

III.1. **Use of *A. vera* in food and food supplements**

There is a lot of potential for *A. vera* in the food and drink industry. In the United States, it is increasingly prevalent for individuals to include powdered extracts into their meals or consume one of the several flavoured *A. vera* beverages. Due to these applications, it appears that *A. vera* is extremely beneficial and has a wide variety of applications (Eshun & Qian, 2004).

A. vera is also utilized in the food sector, primarily in the formulation of health food beverages. Because it has many vitamins and minerals that our bodies need, *A. vera* juice is becoming more popular around the world. It can help with bowel problems and reduce inflammation in the body, like in gout, ear inflammation, and arthritis. *A. vera* is commonly used in fruit drinks combined with other fruits like orange and amla juice. Ready-to-serve (RTS) drinks can be made with *A. vera* juice as a base, along with other fruit juices (Vera et al., 2015).

Additionally, it is utilized in the production of yogurt and other beverages, including tea (Eshun & Qian, 2004). Yogurt, jam, instant tea granules, candy, alcoholic beverages, and ice cream are only few of the food items on the market (Ahlawat & Khatkar, 2011). Desserts made with *A. vera* are both delicious and healthy. Confectionary items often use *A. vera* as an ingredient. Candies, jellies, chocolates, and other sugary treats are included. In a ratio of 40:60, *A. vera* gel and pineapple fruit juice produce a high-quality, nutrient-rich jelly (Palve et al., 2015). The response surface approach was used to find the optimal proportions of each ingredient in the *A. vera* jam making process (Jayabalan & Karthikeyan, 2013). It was reported that up to 20% of *Aloe vera* juice may be used in the manufacturing of ice cream without altering the organoleptic features of the finished product (Manoharan et al., 2012). *A. vera* was used as a functional component in the creation of ice cream in the form of *A. vera* gel concentration, *Aloe vera* cubes, *A. vera* gel powder, and *A. vera* cubes coated in sugar (Ahlawat et al., 2014). *A. vera* is used in many dairy goods, including yogurt, buttermilk, and others. Bioactives can be found in yogurt with *A. vera* gel, which tastes good. *A. vera* yogurt was attempted to be made by (Govindammal et al., 2017). Yogurt that had been supplemented with *A. vera* revealed reduced fat content and more fiber and phytonu-trients such steroids, phlobatannin, saponins, and anthraquinones than the control. Overall, *A. vera* gel-fortified yogurt was excellent, probiotic, and tasty, which may be passed on to consumers. Buttermilk, a dairy drink, has been shown to have significant medicinal and nutritional benefits. To improve its physicochemical, nutritional, and sensory qualities, added *A. vera* juice to buttermilk, which enhanced its viscosity (depending on

the quantity of *Aloe vera* juice). *A. vera* juice fortification of buttermilk improved its nutritional fiber, vitamin C, and iron content (Ahlawat et al., 2014). It has been found that *A. vera* may be used in a variety of baked goods. It can change food rheology and texture as a hydrocolloid. Food manufacturers frequently employ the cellulose and pectic substances found in *A. vera* gel as fat substitutes (Colla et al., 2018). Bread quality and shelf life were both enhanced by adding *A. vera* to the Barbari dough. Adding *Aloe vera* powder of any concentration lengthened the time it took for the dough to absorb water and achieve its full texture. The addition of 9% *A. vera* powder to the dough formulation proved to be the most successful strategy for lowering the extensibility of the dough. Thus, *A. vera* is a useful ingredient for increasing the bread's shelf life (Jafari et al., 2018).

Food supplements are another possible application for *A. vera* (Steenkamp & Stewart, 2007). It is common knowledge that herbal products are generally utilized as dietary supplements with the purpose of either promoting health or preventing illnesses. *Aloe vera* gel can be utilized as an edible covering to preserve the freshness and safety of fresh food (Serrano et al., 2006). The application of *A. vera* gel to table grapes substantially slowed the loss of functional compounds, such as total phenolic and ascorbic acid. In fact, *A. vera* inhibits the proliferation of microorganisms that cause foodborne diseases in humans or animals and food deterioration (Eshun & Qian, 2004). As *A. vera* does not influence food taste or appearance, it may be a safe, natural, and eco-friendly alternative to synthetic preservatives (Serrano et al., 2006). The leaves of Aloe are also consumed as vegetable. In western Rajasthan of India, it is popular to make pickle with small pieces of leaf pad. Unripe flower stalks that don't have any bitterness in them can also be used as vegetables. Green salads, which often include fresh fleshy leaf pads, are often used to treat digestive issues including indigestion and constipation (Langmead et al., 2004).

To extend the freshness of partially cooked chicken nuggets and cold-stored chicken nuggets, application of *A. vera* gel powder was investigated. Chicken nuggets, both partially cooked and cold-stored, may be kept fresh for up to 6 days when *Aloe vera* gel powder is used to reduce the microbial burden (Shahrezaee et al., 2018). Aloe gel powder contains a 14 kDa protein that may inhibit yeast growth (Das et al., 2011). With 2.5% and 3.5% AGP in chicken nugget, it was advised that cooling instead of freezing to extend shelf life by two weeks. Gumming, chewiness, cohesion, hardness, and springiness were all enhanced by *A. vera* gel powder (Shahrezaee et al., 2018). The inclusion of polysaccharides including acemannan, glucomannan, and cellulose in *A. vera* gel powder contributed to the gel's structure and blocked the protein/myofibrils interaction, making the chicken nugget more tender. Since *A. vera* gel powder contributes as a bio-preservative and enhances textural quality indices in meat-based products (Umano et al.1999).

The *A. vera* gel, is loaded in cellulose and pectic compounds, both of which are employed in the food industry as alternatives to fat. It was reported that for the benefit of overweight and obese persons, *A. vera* gel can be used as a fat replacer in the baking process (low fat cream). *A. vera* gel in cakes may help overweight and obese people maintain and/or lose weight while consuming vital *A. vera* gel nutrients (Gutiérrez-Luna et al., 2022).

The Office of Dietary Supplements of the National Institute of Health collects all US dietary supplement label information, such as images of package labels, names and forms of ingredients, amounts of dietary ingredients, and all label statements, in the Dietary Supplement Label Database. It provides a comprehensive list of 43 products that use *A. vera* as an active component, with varying quantities ranging from 0.33 to 750 mg per capsule. Dietary supplements made from *A. vera* whole leaf extract (which includes both the gel and latex) and *A. vera* decolorized whole leaf extract (from which most of the latex components have been removed) are widely used to treat a wide range of systemic diseases. Both aloe-emodin and aloin A, the primary anthraquinone components of *A. vera* latex, appear to be present in varying concentrations throughout different products (NLM, 2012).

In compliance with acceptable manufacturing standards, the US-FDA has authorized *A. vera* to be used as a food flavouring agent (Ulbricht et al., 2008). There are a number of health beverages on the market made from bottled *A. vera* juice, both pure and mixed with various fruit juices. Because of its bitter taste, *A. vera* juice is typically combined with other flavorful ingredients in order to make it more palatable, such as lemon juice, electrolyte, soluble fiber, amino acids and acetaminophen, vitamin B, yoghurts, vegetable juice, tropical fruit juice, and cucumber juice (Pandey & Singh, 2016; Hamman, 2008; Foster et al., 2011). As an alternative, vacuum evaporation can be used to create a concentrate of *A. vera* that retains all its bioactive ingredients without the need of any preservatives (Singh et al., 2011; Singh & Shalini, 2014). *A. vera* concentration is preferable for jams and jellies because to its consistency. It also contains tea, juice, and water for intestinal cleaning and weight loss (Ahlawat & Khatkar, 2011; Medina-Torres et al., 2016). The use of *A. vera* powder as a dietary supplement to increase the body's natural antioxidant defenses is a growing trend (Eshun & Qian, 2004; Kumar et al., 2017a).

III.2. Use of *Aloe vera* in medicines

In the 1930s, *A. vera* gained popularity in the US due to its beneficial use in treating X-ray burns with freshly cut leaves. Both gel and latex *Aloe vera* leaf derivatives have diverse medicinal properties (Ro et al., 2000). According to the World Health Organization, *Aloe vera* latex has been shown to be effective in treating occasional constipation (Surjushe et al., 2008).

A. vera demonstrated properties in promoting wound healing. A mannose-rich polysaccharide called glucomannan and a growth hormone called gibberellin interact with growth factor receptors on the fibroblast to stimulate its activity and proliferation, which increases collagen synthesis after topical and oral *A. vera* (Chithra et al., 1998a). Collagen content, collagen composition (more type III), and collagen cross linking were all improved by A. gel treatment of the wound. This accelerated wound contraction and strengthened scar tissue (Heggers et al., 1996). It has been reported that oral or topical treatment stimulates an increase in hyaluronic acid and dermatan sulfate synthesis in the granulation tissue of a healing wound (Chithra et al., 1998b).

Various chemicals in *A. vera*, such as alkaloids, glycosides, phenolic substances, flavonoids, saponin glycosides, and anthraquinones, have been shown to have antioxidant properties (Kumar et al., 2017b). Studies have demonstrated that it can improve overall antioxidant capacity in plasma, decrease formation of reactive oxygen species (ROS), and scavenge free radicals (Cesar et al., 2018). The presence of these antioxidant activities hints at the possible health advantages of *A. vera* in protecting cells from oxidative damage (Sun et al., 2017). The antioxidant effects of *A. vera* were also found in mouse model tests, which were fed routinely with plant leaves (Raksha et al., 2014; Hęś et al., 2019).

A. vera's antiseptic properties come from the presence of lupeol, salicylic acid, urea nitrogen, cinnamonic acid, phenols, and sulfur. Each one inhibits the growth of bacteria, viruses, and other microorganisms (West & Zhu, 2003).

A. vera prevents the development of bacteria responsible for foodborne sickness in people or animals as well as food deterioration (Eshun & Qian, 2004).

There was significant antibacterial action against *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, and *Salmonella typhi*, and high antimycobacterial activity against *Mycobacterium TB* in the *Aloe vera* extract. Two types of bacteria, *Streptococcus pyogenes* and *Streptococcus faecalis*, have been shown to be suppressed by *Aloe vera* gel (Djeraba & Quere, 2000). *Malassezia furfur* growth on Sabouraud's dextrose agar medium was progressively suppressed, demonstrating antifungal activity. *Candida albicans* growth was slowed by a processed *A. vera* gel formulation (Rezazadeh et al., 2016). Among the species tried, *A. vera* proved to be the most effective (Parihar et al., 2006). The evaluation of the effects of *A. vera* on the mycelium development of *Rhizoctonia solani* and *Colletotrichum coccodes* revealed that the pulp of *A. vera* had an inhibitory impact, slowing the rate of colony formation (Rodríguez et al., 2005).

Many anthraquinones attack encapsulated viruses (Alves et al., 2004). Direct inhibition of cytomegalovirus growth in cell culture was shown using lectins, a portion of *A. vera* gel. It has been

shown that aloe emodin may inhibit the infectiousness of herpes simplex virus and that it can inactivate all viruses, including influenza and pseudorabies (Sadeghi et al., 2015).

Several components of *A. vera*, including its inorganic elements (vanadium, manganese, and copper), and notably its polysaccharides, may play an important role in the plant's antidiabetic properties (Rajendran et al., 2007; Vienna et al., 2005). This plant has been related to decrease blood glucose levels in diabetics and lower cholesterol levels (about 30% lower) in hyperlipidaemic individuals (Geremias et al., 2006; Lim et al., 2003).

Numerous research has examined *A. vera*'s anti-cancer capabilities (Hussain et al., 2015). Successful results have been seen in both in vitro and in vivo studies (Lim et al., 2003; Chen et al., 2016; Tseng et al., 2017; Trybus et al., 2018). Breast, cervical, digestive, and melanoma cell lines have all been shown to be inhibited by *Aloe vera* extracts and isolated component aloe-emodin (Hussain et al., 2015; Liu et al., 2018; Chang et al., 2016; Xu & Xu, 2016; Rawla et al., 2019; Chen et al., 2018; Chihara et al., 2015; Ali et al., 2013; Tabolacci et al., 2015). Potential therapeutic uses in the fight against cancer are suggested by these results. While preclinical research shows its usefulness, rigorous clinical trials are needed to confirm *A. vera*'s anti-cancer potential in humans (Damani et al., 2015; Koo et al., 2019).

Salicylic acid, an analgetic and anti-inflammatory, inhibits prostaglandin formation from arachidonic acid, creating anti-inflammatory and immunological benefits (Davis et al., 1991). Therefore, A. has been utilized to aid with arthritis and other joint-related issues. The presence of A. polysaccharides has been found to increase immune function (Choi & Chung, 2003; Yu et al., 2009; Vienna et al., 2005; Zhang et al., 1996).

According to several studies (Roberts & Travis, 1995; Sato et al, 1990), *A. vera* gel can prevent skin damage. Although its precise function is unclear, topical application of *Aloe vera* gel has been shown to induce the production of the antioxidant protein metallothionein in the skin, which acts as a scavenger for hydroxyl radicals and a protector against the downregulation of superoxide dismutase and glutathione peroxidase. It inhibits UV-induced inhibition of delayed type hypersensitivity by reducing skin keratinocyte-derived immunosuppressive cytokines such interlukin-10 (Byeon et al., 1998).

A. vera latex is commonly used in the treatment of constipation (de Witte, 1993); the laxative effect of the anthraquinone glycosides found in *A. vera* latex is well established (Ulbricht et al., 2008). In a double-blind, randomized, controlled trial of 28 healthy adults, aloin was reported to have a laxative effect compared to a placebo that was stronger than the stimulant laxative phenolphthalein (Chapman & Pittelli, 1974). In subjects with chronic constipation, a novel preparation containing *A. vera*, celandine, and psyllium was found to improve a range of constipation indicators (bowel movement

frequency, consistency of stools, and laxative dependence) in a 28-day double-blind trial; however, the effect of *Aloe vera* alone was not investigated in this study (Odes & Madar, 1991). *A. vera* laxative preparations have been approved by the German Commission and governmental regulatory agency for use in the treatment of constipation as a second-line agent; however, *A. vera* latex is no longer recognized as an over-the-counter drug by the U.S. Food and Drug Administration due to a lack of sufficient data to establish its safety for use as a laxative.

Consuming *A. vera* juice delivers a rich combination of vitamins, minerals, and trace elements that can assist our bodies in coping with the stresses and strains that are experienced daily. *A. vera* juice is an excellent natural help to detox (Mawase et al., 2016).

A. vera juice is highly useful in the treatment of ulcers, heartburn, and other gastrointestinal problems. *Aloe vera* may also be useful for kids, according to recent studies (Ortiz & Clauson, 2006). This effect of *Aloe vera* extract on acid secretion may be attributable to the presence of lectins in the plant. It has been demonstrated that lectins block aminopyrine absorption by parietal cells; hence, the capacity of the extract to decrease gastric acid output may be as a consequence of direct action on the cells that produce acid (Borra et al., 2011).

The leading cause of heart attacks and strokes is high blood cholesterol. Effect of *A. vera* extract on blood cholesterol in male rats was investigated (Chandrakar et al., 2008). Serum cholesterol levels were found to be significantly reduced in all aloes vera-treated rat groups, with the significance level being 5% for the dose of 6 mg/kg and 0.1%, 0.5%, and 0.2%, respectively. It was found that *Aloe vera* consumption was associated with reduced inflammation and cholesterol levels, two major risk factors for atherosclerosis (Dana et al., 2012). In addition, studies using *A. vera* gel extract administered orally to diabetic rats at a dosage of 300 mg/kg body weight per day for 21 days shown a substantial decrease in cholesterol and triglyceride levels in blood plasma (Rajasekaran et al., 2006).

The possible preventive impact of isolated *A. vera* chemicals on bone pathogenesis has been the focus of in vitro investigations. Activation of the bone morphogenetic protein 2 (BMP-2) and mitogen-activated protein kinase (MAPK) signaling pathways by aloe-emodin in clonal mouse chondrogenic ATDC5 cells (Yang et al., 2016; Pengjam et al., 2016; Madhyastha et al., 2018).

III.3. Use of *Aloe vera* in cosmetics

Aloe vera helps keep skin looking young by boosting collagen and elastin production.

Soaps, shampoos, creams, and lotions containing *Aloe vera* are widely available for use as cosmetics. *Aloe vera* gel has been shown to diminish the depth of pigmentation and lighten dark spots on the face. Applying the gel topically not only hydrates the skin but also exfoliates dead skin and revitalizes the skin. And it helps repair dry, brittle locks. This gel can help stop the development of acne and

pimples on oily skin types. Antioxidants in this plant have been shown to reduce the appearance of aging symptoms including scarring and scratch marks (Rajeswari et al., 2012).

A. vera gel is a great cosmetic and dermatological component, and it is used in more than 95% of the dermatological treatments that are created all over the world. In the United States, the Food and Drug Administration (FDA) has authorized the topical use of *Aloe vera* gel in cosmetic products (Javed & Atta-ur-rahman, 2014). There are a wide variety of *A. vera*-based cosmetics available, with concentrations ranging from 1 to 98%. It is commonly known that *A. vera* gel, which gives the plant the ability to retain moisture for very extended periods of time, also possesses calming effects (Bhat et al., 2011). The use of *A. vera* in cosmetics is often done more for aesthetic purposes (i.e., to add a touch of "nature" to the product) than for any therapeutic ones, and the amount used is sometimes rather minimal (Javed & Atta-ur-rahman, 2014). In the cosmetics business, the gel is utilized as a moisturizing component in a wide variety of products including lotions, creams, sun lotions, shaving creams, lip balms, therapeutic ointments, and face packs (Eshun & Qian, 2004). Products including mouthwash, hair tonic, shampoo, and skin-moisturizing gel also include *A. vera* (Javed & Atta-ur-rahman, 2014). Anthraquinone-enriched Anthraquinones, which are found in *Aloe vera* extracts, absorb ultraviolet radiation. This means that *A. vera* extracts could be used in sunscreens to absorb UV radiation (Javed & Atta-ur-rahman, 2014). Studies on both short- and long-term use of formulations containing freeze-dried *Aloe vera* extract found that the extract was effective in increasing skin moisture via a humectant mechanism (Dal'Belo et al., 2006).

CHAPTER IV

REGULATORY FRAMEWORK ON THE USAGE OF *ALOE VERA* IN THE EUROPEAN UNION

IV.1. General information

In the 1600s, *Aloe vera* cultivation by Spain and the Netherlands on Caribbean islands reached Europe (Singh & Françozo, 2023). *A. vera*, a plant with a long history in pharmacopeia, was initially recorded in Germany around the 12th century. Since that time, 20 different countries have included it in their national pharmacopeias as a laxative. Following extensive investigation into *A. vera's* properties and efficacy, the plant has been used in a wide variety of medicinal contexts. Beginning in the 1970s in the United States and some European countries*, Aloe vera* gel extracts were included in health foods and drinks and moisturizing cosmetics (Park & Jo, 2006; Dybka-Stępień et al., 2021). A lot of different botanicals, preparations, and derivatives are used in products and marketed as being good for your health and body. Foods, dietary supplements, cosmetics, pharmaceuticals, and medical devices all fall into this category. Different product groups have different legal requirements that affect how the effectiveness of these effects is measured and recorded (EAS, 2008; Colombo et al., 2020).

IV.2. Aloe vera in and as food supplement under Directive 2002/46/EC

According to the Directive 2002/46/EC, food supplements means foodstuffs the purpose of which is to supplement the normal diet and which are concentrated sources of nutrients or other substances with a nutritional or physiological effect, alone or in combination, marketed in dose form, namely forms such as capsules, pastilles, tablets, pills and other similar forms, sachets of powder, ampoules of liquids, drop dispensing bottles, and other similar forms of liquids and powders designed to be taken in measured small unit quantities. Member States must make sure that food supplements can only be sold in the European Union if they follow the rules in this Directive (Directive 2002/46/EC). The labelling, presentation and advertising must not attribute to food supplements the property of preventing, treating or curing a human disease, or refer to such properties (Directive 2002/46/EC). No food supplement label, presentation, or promotion may state or imply that a balanced and diverse diet cannot offer enough nutrients (Directive 2002/46/EC). On the label, the amount of nutrients or chemicals that have a physiological or nutritional effect that are in the product must be written in number form (Directive 2002/46/EC). *Aloe vera* is often used in food supplements, and these products are subject to the EU's regulatory framework for food supplements outlined in Directive 2002/46/EC.

Aloe vera-contained in supplements must comply with the composition requirements specified in the directive (Rao et al., 2022). It is obligatory to have clear and accurate labelling for food supplements containing *Aloe vera*. This includes providing information on the *Aloe vera* content and any potential allergens (Khan et al., 2021).

IV.3. *Aloe vera* under the health claim regulation…

Health claims related to *Aloe vera* in these supplements must comply with the Regulation (EC) No. 1924/2006[1] concerning nutrition and health claims made on foods. Regulation (EC) No 1924/2006 harmonises nutrition and health claim laws, regulations, and administrative actions in Member States to guarantee the internal market's efficiency and consumer protection. This Regulation applies to nutrition and health claims in commercial communications, such as labelling, presentation, or promotion of goods available to consumers. Nutritional and health claims can only be used on the labels, packaging, and advertising of foods placed on the market in the European Community if they follow the rules set out in the Regulation itself. As long as Regulation (EU) no 1169/2011 on food information to consumers and Directive 2006/114/EC are followed, nutrition and health claims must not: (a) be fake, unclear, or confusing; (b) make people question the safety and/or nutritional value of other foods; or (c) encourage or allow people to eat too much of a food.

Up till now, no health claims for *Aloe vera* have been authorised under the health claim regulation, in the European Union.

IV.4. … and under Regulation (EC) no 1925/2006

The steps of article 8 in chapter III of Regulation (EC) No 1925/2006 of the European Parliament and of the Council "*on the addition of vitamins and minerals and of certain other substances to foods*", must be followed also when a substance that isn't a vitamin or mineral or an ingredient that contains a substance that isn't a vitamin or mineral is added to foods or used to make foods in a way that would cause people to eat much larger amounts of that substance than they would normally eat when eating a balanced and varied diet, or when the food would otherwise contain large amounts of that substance (see Regulation (EC) No 1925/2006). The Commission has the authority to make decisions to modify non-essential aspects of this Regulation, either independently or based on information provided by Member States. Before making such decisions, the Commission must assess the available information in consultation with the Authority, following the regulatory procedure with scrutiny as outlined in

[1] Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods.

Article 14(3). These decisions may involve the inclusion of the substance or ingredient in Annex III, if regarded necessary. Specifically:

"(*a) if a harmful effect on health has been identified, the substance and/or the ingredient containing the substance shall:*

(i) be placed in Annex III, Part A, and its addition to foods or its use in the manufacture of foods shall be prohibited; or

(ii) be placed in Annex III, Part B, and its addition to foods or its use in the manufacture of foods shall only be allowed under the conditions specified therein;

(b) if the possibility of harmful effects on health is identified but scientific uncertainty persists, the substance shall be placed in Annex III, Part C".

Regulation (EC) No 2021/468 has made changes to Annex III to Regulation (EC) no 1925/2006. In one part of the list (Part A), they added new items in alphabetical order, such as substances like "aloe-emodin", "emodin", and certain preparations containing them. Another addition is "*preparations from the leaf of Aloe species containing hydroxyanthracene derivatives*" and "*danthron and all preparations in which this substance is present*". In another part of the list (Part C), new entries include things like "*preparations from the root or rhizome of Rheum palmatum L., Rheum officinale Baillon and their hybrids containing hydroxyanthracene derivatives*", "*preparations from the leaf or fruit of Cassia senna L. containing hydroxyanthracene derivatives*", and "*preparations from the bark of Rhamnus frangula L., Rhamnus purshiana DC. containing hydroxyanthracene derivatives*". These changes are part of the regulation's effort to manage and control certain substances in products.

The European Food Safety Authority (EFSA) works to ensure "*Safety in the food chain from farm to fork*". EFSA's main goal, like the FDA's in the US, is to keep food chains in Europe as safe as possible. EFSA gives policymakers independent and clear scientific advice by working with partners and having open conversations with society (Pressman et al., 2022).

The EFSA Panel on Dietetics products, Nutrition and Allergies (NDA) was asked to provide an opinion on the scientific basis of a health claim related to hydroxyanthracene derivatives and bowl function after Vivatech applied for authorisation under Article 13(5) of Regulation (EC) no 1924/2006, via the competent Authority of France. Transitech was a food supplement subject to health claim. The Panel acknowledges the short-term pain relief provided by hydroxyanthracene derivatives extracted from *Aloe barbadensis Miller* and/or various aloe species, mainly *Aloe ferox Miller*, at the proposed condition of use i.e 10 mg/day. The Panel finds a link between hydroxyanthracene compounds and positive bowl function (European Food Safety Authority, 2013). One EU Member State highlighted concerns about the side effects of eating foods containing hydroxyanthracene derivatives and preparations, such as dietary supplements. EFSA was asked to

review the scientific data on the possible link between hydroxyanthracene derivative intake and harmful health effects and to recommend a daily intake that does not raise health concerns for the general population and subgroups, including vulnerable groups (European Food Safety Authority, 2018). The EFSA issued a public call for data from food business operators on many subjects relating to dietary supplements containing hydroxyanthracene derivatives. The EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS Panel) assessed the risk on the basis of the 2009 EFSA Guidance on safety evaluation of botanicals and botanical preparations for food supplements. The Panel highlighted that aloe-emodin and emodin exposure is unknown due to a lack of evidence. The opinion "*Safety of hydroxyanthracene derivatives for use in food*" evaluates human and animal research (European Food Safety Authority, 2018). The Panel concluded that hydroxyanthracene derivatives are genotoxic and carcinogenic unless there is specific data to the contrary. The Panel also failed to recommend a daily intake of hydroxyanthracene derivatives that would not affect the general population or susceptible subgroups (European Food Safety Authority, 2018). Considering the severe health risks associated with these derivatives, especially aloe-emodin, emodin, danthron, and aloe extracts, the decision was to prohibit their use in food, placing them in Annex III, Part A of Regulation (EC) No. 1925/2006 (European Food Safety Authority, 2018).

IV.5. Aloe vera and the novel food Regulation

Novel food refers to food products that have not been traditionally consumed and are relatively new to the market and offers unique and new qualities. It includes new ingredients, which have gained popularity in recent years (Pisanello & Caruso, 2018). The provisions governing novel foods within the European Union were introduced with the adoption of Regulation (EC) No. 258/97[2] by the European Parliament and the Council, as well as Commission Regulation (EC) No. 1852/2001[3]. The aforementioned regulation were repealed by Regulation (EU) 2015/2283[4], adopted in order to include recent modifications in Union legislation and improvements in technology, as well as to enhance the efficiency of the current authorization procedures. According to Article (3) of Regulation (EU) No.

[2] Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients.

[3] Commission Regulation (EC) No 1852/2001 of 20 September 2001 laying down detailed rules for making certain information available to the public and for the protection of information submitted pursuant to European Parliament and Council Regulation (EC) No 258/97.

[4] Regulation (EU) 2015/2283 of the European Parliament and of the Council of 25 November 2015 on novel foods, amending Regulation (EU) No 1169/2011 of the European Parliament and of the Council and repealing Regulation (EC) No 258/97 of the European Parliament and of the Council and Commission Regulation (EC) No 1852/2001.

2015/2283 a food is considered novel if it was not generally used for human consumption in the Union before 15 May 1997 and if it falls under one of the categories listed by the Regulation. However, due to scientific and technical advances since 1997, the novel food categories once listed in the old novel food regulation had to be reviewed, clarified, and updated. Under Regulation (EU) 2015/2283 the categories include

i) food with a new or intentionally modified molecular structure, where that structure was not used as, or in, a food within the Union before 15 May 1997;

(ii) food consisting of, isolated from or produced from microorganisms, fungi or algae;

(iii) food consisting of, isolated from or produced from material of mineral origin;

(iv) food consisting of, isolated from or produced from plants or their parts, except when the food has a history of safe food use within the Union and is consisting of, isolated from or produced from a plant or a variety of the same species obtained by:

— traditional propagating practices which have been used for food production within the Union before 15 May 1997; or

— non-traditional propagating practices which have not been used for food production within the Union before 15 May 1997, where those practices do not give rise to significant changes in the composition or structure of the food affecting its nutritional value, metabolism or level of undesirable substances;

(v) food consisting of, isolated from or produced from animals or their parts, except for animals obtained by traditional breeding practices which have been used for food production within the Union before 15 May 1997 and the food from those animals has a history of safe food use within the Union;

(vi) food consisting of, isolated from or produced from cell culture or tissue culture derived from animals, plants, micro-organisms, fungi or algae;

(vii) food resulting from a production process not used for food production within the Union before 15 May 1997, which gives rise to significant changes in the composition or structure of a food, affecting its nutritional value, metabolism or level of undesirable substances;

(viii) food consisting of engineered nanomaterials;

(ix) vitamins, minerals and other substances used in accordance with Directive 2002/46/EC, Regulation (EC) No 1925/2006 or Regulation (EU) No 609/2013, where:

— a production process not used for food production within the Union before 15 May 1997 has been applied; or

— they contain or consist of engineered nanomaterials;

(x) food used exclusively in food supplements within the Union before 15 May 1997, where it is intended to be used in foods other than food supplements.

Whether a food was utilized for human consumption to a considerable degree in the Union before 15 May 1997 should be based on food business operator information and maybe additional Member State information. If they are unclear about the item's status, food businesses should ask Member States under the Article (4) of Regulation (EU) 2015/2283. Article 7 of the Regulation "General conditions for inclusion of novel foods in the Union list" states that novel foods shall only be approved and used if they meet Regulation (EU) 2015/2283. If the safety of a novel food cannot be determined and scientific ambiguity remains, the precautionary principle may be used. No customer should be misled by their usage. Therefore, where a novel food is intended to replace another food, it should not differ from that food in a way that would be nutritionally less advantageous for the consumer. (art. 7(c), Regulation (EU) 2015/2283). Novel foods should not be sold or utilized in food for human consumption unless they are on the Union list of authorized novel foods. Article 8 of Regulation (EU) 2015/2283 mentions that the Union list should include novel foods previously permitted or notified under Regulation (EC) No 258/97, including any existing authorisation requirements, by an implementing act. The Union list of novel foods that can be sold in the Union, as described in Article 6 of Regulation (EU) 2015/2283, was made public and could be found in the Annex to Regulation (EU) 2017/2470[5], amended by the Annex to Commission Implementing Regulation (EU) 2018/1023[6] and by any implementing regulations which authorises a novel food. This regulation considers *Aloe macroclada Baker* leaf extract under authorised novel food with following conditions under which it may be used. The product should only be used in the food category of Food Supplements as defined in Directive 2002/46/EC, and the maximum limit that should be used is "*In line with normal use in food supplements of the similar gel derived from Aloe vera (L.) Burm*". In addition, this regulation provides specifications on the *Aloe macroclada Baker* leaf extract as "*powdered gel extract derived from the leaves of Aloe macroclada Baker which is substantially equivalent to the same gel derived from Aloe vera (L.) Burm.f. leaves with Ash: 25%, Fiber content in the diet: 28.6%, Fat: 2,7%, Water content: 4.7%, Total sugars: 9,5%, Total Protein Content: 1.63%, 8.9% Glucose*".

Novel food safety risk assessment criteria should also be established. Novel food scientific assessments should be done by the European Food Safety Authority to guarantee harmonisation. If the proposed change to the Union list is likely to have an impact on human health, EFSA should be

[5] Commission Implementing Regulation (EU) 2017/2470 of 20 December 2017 establishing the Union list of novel foods in accordance with Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods.

[6] Commission Implementing Regulation (EU) 2018/1023 of 23 July 2018 correcting Implementing Regulation (EU) 2017/2470 establishing the Union list of novel foods.

asked for its view as part of the procedure for authorizing a novel food. EFSA should evaluate any novel food qualities that may constitute a health risk to humans and their consequences on vulnerable populations.

IV.6. *Aloe vera* and the food flavouring Regulation

Article 3 of Regulation (EC) No. 1334/2008 defines the term flavouring as either products *"not intended to be consumed as such, which are added to food in order to impart or modify odour and/or taste"* or products *"made or consisting of the following categories: flavouring substances, flavouring preparations, thermal process flavourings, smoke flavourings, flavour precursors or other flavourings or mixtures thereof*". Article 3 further describes food ingredient with flavouring properties, "*a food ingredient other than flavourings which may be added to food for the main purpose of adding flavour to it or modifying its flavour and which contributes significantly to the presence in food of certain naturally occurring undesirable substances*". Under article 4, general conditions for the use of flavourings or food ingredients with flavouring properties are listed according to which flavourings or food ingredients with flavouring properties can only be used in food if they do not pose a safety risk to consumer's health on the basis of available scientific evidence and their use should not mis lead consumers. 15 substances including Aloin, which shall not be added as such to food, are specified in Part A of Annex III (Demyttenaere, 2011; Kaparakou et al., 2020).

IV.7. Aloe and cosmetics

A list of chemicals must be on the label of cosmetics according to Article 19(1)(g) of Regulation (EC) No. 1223/2009[7]. The Commission must create and maintain an inventory of common ingredient names under Article (33) of the Regulation. The list needs to include names that are used all over the world, like the International Nomenclature of Cosmetic Ingredients (INCI). Article (33), of Regulation (EC) No. 1223/2009 says that the glossary's common ingredient names must be used on cosmetics labels no later than 12 months after the glossary is published in the Official Journal of the European Union.

The list of common ingredient names was made by Commission Decision (EU) No. 2019/701[8] in line with Article 33 of Regulation (EC) No. 1223/2009 repealed by Decision (EU) No. 2019/701. The glossary of Commission Decision (EU) No. 2022/677 specifies that common component names and

[7] Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products.

[8] Commission Decision (EU) 2019/701 of 5 April 2019 establishing a glossary of common ingredient names for use in the labelling of cosmetic products.

the way they are present must be made evident on cosmetic product labels. In the case of *Aloe vera*, it was made clear what form, part, or combination of *Aloe vera* was used in the cosmetic. Here are some *Aloe vera* ingredients and how to present them on cosmetic items: “Aloe Barbadensis Callus Culture Extract, Aloe Barbadensis Callus Extract, Aloe Barbadensis Callus Powder, Aloe Barbadensis Extract, Aloe Barbadensis Flower Extract, Aloe Barbadensis Leaf, Aloe Barbadensis Leaf Extract, Aloe Barbadensis Leaf Juice, Aloe Barbadensis Leaf Juice Powder, Aloe Barbadensis Leaf Polysaccharides, aloe barbadensis Leaf powder, Aloe Barbadensis Leaf Water, Aloe Barbadensis Leaf/Sucrose Ferment Filtrate, Aloe Barbadensis Phytoplacenta Extract, Aloe Barbadensis Sprout, *Aloe vera* Callus Extract, *Aloe vera* Leaf Extract, *Aloe vera* Vesicles”. In the complex landscape of cosmetic regulations in the European Union, transparency regarding potential allergens is essential. A crucial requirement mandates clear labeling of potential allergens on product labels, demonstrating the EU’s commitment to consumer safety and recognition of diverse sensitivities. Potential allergens encompass various ingredients that may trigger allergic reactions, including common elements like fragrances, preservatives, or specific plant extracts, such as *Aloe vera*. By enforcing clear labeling, regulatory authorities empower consumers to make informed choices, particularly if they have known sensitivities or allergies (Pistollato et al., 2021).

CHAPTER V
CONCLUDING REMARKS

Aloe vera is a versatile succulent renowned for its diverse applications in food, cosmetics, and traditional medicine. We discussed aloe gel's toxicological properties in detail and quickly go over the chemical makeup of different aloe preparations.

To ensure safe commercial use, further toxicological studies on Aloe gel are needed to establish the maximum allowable concentration of harmful substances (HADs) without inducing toxicity and the optimal treatment duration. Ongoing market surveillance is crucial, involving monitoring of HADs content in Aloe products. In the absence of official analytical methods, leveraging existing literature can guide the development of validated analytical methods, essential for both Food Companies and Competent Authorities in EU countries. Standardized procedures will facilitate reliable monitoring of the chemical composition of Aloe extracts, ensuring comparability. Lastly, to minimize HADs contamination from mesophyll and rind tissues, manufacturers should establish efficient Standard Operating Procedures (SOPs) for extraction and decolorization that are both feasible and scalable.

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