ISAR Journal of Medical and Pharmaceutical Sciences
Vol-2, Iss-9 (Sep- 2024)
Abbriviate Title- ISAR J Med Pharm Sci
ISSN *(Online)*- 2584-0150
https://isarpublisher.com/journal/isarjmps

QUALITY CONTROL STUDIES IN THE TURKEY MARKET ON SOFT GELATIN CAPSULES CONTAINING CHIA (SALVIA *HISPANICA L.*) SEEDS OIL

Ebru Derici Eker[1*], Mohammed Yahia Asaad[2]

Mersin University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Mersin, Türkiye.

***Corresponding Author**
Ebru Derici Eker

Mersin University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Mersin, Türkiye.

Article History
Received: 14.08.2024
Accepted: 05.09.2024
Published: 21.09.2024

Abstract: - Chia seed, which has its origins in prehistoric times, is a food that has become popular as a superfood with its high content of oil, protein and dietary fiber. Chia seeds contain 17-24% protein, 18-30% fiber and 25-40% fat. 80% of the oil content of the seed consists of α-linolenic acid (omega-3) and linoleic acid (omega-6). Since the preparations available in the market in our country are put on the market with the permission of the Ministry of Agriculture, they do not need to pass *in vitro* and *in vivo* efficacy, safety and quality control tests like the human drugs licensed by the Ministry of Health. In our study, it is aimed to evaluate the quality control of chia seed oils and soft capsule formulations with different formulations marketed by different companies in the Turkish market. Determination of organoleptic properties, weight deviation, disintegration test, dissolution test, DPPH antioxidant capacity measurement and phenolic substance determination analyzes were performed on soft gelatin capsules containing chia seed oil and oils. According to the data obtained, the capsules are suitable in terms of organoleptic properties. The mean weight deviation of soft gelatin capsules was 0.7283±0.024g for sample A and 1.2947±0.015g for sample B. According to the results obtained from the disintegration test, the capsules dispersed between 5 minutes 14 seconds and 6 minutes 32 seconds in the artificial stomach medium, between 5 minutes 14 seconds and 6 minutes 32 seconds in the artificial gut medium, and between 16 minutes 2 seconds and 18 minutes 30 seconds in pure water. We think that its use as an herbal supplement would be appropriate due to the results in accordance with the literature in quality control tests on soft gelatin capsules and oils containing chia seed oil.

Keywords: *Salvia hispanica L.* (chia seeds oil), omega-3, soft gelatin capsule, quality control.

Cite this article:

Eker, E. D., Asaad, M. Y., (2024). QUALITY CONTROL STUDIES IN THE TURKEY MARKET ON SOFT GELATIN CAPSULES CONTAINING CHIA (SALVIA *HISPANICA L.*) SEEDS OIL. *ISAR Journal of Medical and Pharmaceutical Sciences*, *2*(9), 61-69.

Introduction

Chia is a word of Spanish origin, originating from the word chien, meaning fatty. It is an annual plant originating from Mexico and Guatemala and is a member of the *Lamiaceae* family (Mint family), also known as Salba [1]. It has been used as food since 3500 BC. This small seed, which was the main source of nutrition and energy for humans and animals by the Aztecs and Mayans, is not only used in food but also in medicines and is used in the food industry [2,3].

In a wide variety of folk remedies, primary cosmetics, and religious rituals of pre-Columbian societies in the Americas and Mexico [1]. It is commercially grown today in Peru, Argentina, Paraguay, Mexico, Bolivia, Australia, Guatemala, Nicaragua and Ecuador [3].

Chia seeds contain 18-30% dietary fiber, 26-41% carbohydrates, 25-40% fat, 15-20% protein and 90-93% a wide variety of polyphenols. One of the most important antioxidant phenolic components of chia seeds is tocopherols. The high proportion of phenolic components consists of caffeic acid, chlorogenic acid, quercetin and kaempferol. These components have been reported to have a much higher antioxidant effect than substances with high antioxidant properties, such as vitamin E, ferulic acid and vitamin C [1–9].

Chia seeds provide approximately 486 kcal of energy. Chia seeds are a food rich in calcium, phosphorus, potassium, magnesium, sodium, iron and zinc [2]. It has been determined that the heavy metal content of the seeds is within safe limits and is free of mycotoxins. Moreover, although it is insufficient in vitamin C, it is very rich in vitamins B1, B2, B3, B6, A, E and K [10]. One of the most important features of chia seeds is that they do not contain gluten. Therefore, it is a safe alternative food source for celiac patients and individuals with gluten sensitivity [9]. However, it should not be forgotten that the nutritional content of the chia plant may vary depending on growing conditions and soil characteristics [11].

Chia seeds are truly an excellent source of protein for people who eat little or no animal products. In recent years, health has become very popular with the public. Many studies have shown that chia increases the nutritional quality of foods and is used as a raw

***Corresponding Author: Ebru Derici Eker**

material in the food industry. It is known that the components it contains are very useful in a wide spectrum ranging from cancer to cardiovascular diseases and diabetes. It has been reported that it has a supportive effect on the digestive and immune systems [4-5].

In our country, Chia can be used safely without any potentially harmful effects. Chia seeds are generally consumed raw. Its most common use is in baked goods, nutritional supplements, cereal bars, cookies, breads, oatmeal, yogurt, salads and added to foods. Chia seeds can also be used as a spice by adding them to soups and sauces [6-7].

Chia seeds Its preparations in Turkey are: Naturoil Chia Seed Oil, Alfacol chia seed capsule, Desteque Chia Seed Soft Capsule, Zade Vital Chia Seed Oil Capsule, Tabiat Market Chia Seed Oil, Balen Kiya Chia Seed Oil, Qatre Premium Chia Seed Oil, Herbs & Oils Chia Seed Oil, Modern Aktar Chia Seed Oil, Zade Vital Chia Seed Oil [8].

Faulty eating habits today cause an increase in many diseases such as diabetes, hypertension, cardiovascular diseases and cancer. It is also known that excessive amounts of saturated fatty acids consumed in the diet cause high cholesterol and cardiovascular diseases. Therefore, there is an increasing demand for chia seeds to be included in the diet. Since chia seeds contain functional food components, many clinical studies have been conducted and continue to be conducted regarding their effects on health. Clinical studies show that regular consumption of chia seeds is an alternative food source that has a protective effect on the body against cancer, obesity, diabetes and cardiovascular diseases [12].

In general, the stability of tablets and capsules depends on the physical and chemical properties of the formulations. Both stability properties cannot be examined independently of each other. For this reason, first of all, the physical and chemical properties of the substances that make up the formulation should be well known. For example, the hygroscopic structure of the active ingredient in tablets and capsules, the presence or absence of polymorphic crystal forms, melting point, pKa value, solubility, degradation mechanisms, etc. Then, the effects of temperature, humidity and light, interactions with the active ingredient and excipients, as well as possible interactions between the active ingredient and excipients in the capsules and the capsule sheath should be investigated. During capsule formulation development and filling of capsules, a series of quality control tests are carried out to ensure that the capsules produced meet the specified requirements.

These tests occur in three stages:

A. Controls of starting materials (identification, purity, potency, quantity determination, particle size distribution and shape of solids, moisture determination, etc.)

B. In-process and intermediate product (powders or granules) controls

C. Finished product controls

A. Controls of starting materials

All components of the softgel dosage form are checked and tested to ensure compliance with pharmacopeial specifications. Additional specification tests may be added for certain excipients to ensure manufacture of a high quality softgel product. For example, it is important to limit certain trace impurities such as aldehydes and peroxides that may be present in polyethylene glycol. The presence of high levels of these impurities leads to cross-linking of the gelatin polymer, leading to insolubility through further polymerization. With long-term storage, this may lead to slow dissolution of the capsule shell and subsequent delayed drug release. Gelatin also requires careful control of quality to ensure a manufacturable and stable product. The quality of gelatin is controlled using parameters such as the viscosity of a hot solution and the blooming strength of the gel. Bloom power is a measure of gel hardness.

B. In - process controls

- Sheath strip thickness
- Thickness of the soft gel seal at the time of encapsulation
- Weight of filled matrix and weight of capsule wall
- Moisture level of the soft gel wall and hardness of the soft gel at the end of the drying phase

Appropriate control levels for these parameters are determined during process development for each softgel product and implemented in routine production-scale manufacturing.

C. The controls performed on the finished product Capsules are given below:

1. Organoleptic properties (colouration, appearance, cracking, shrinkage, stickiness)
2. Active ingredient quantification
3. Weight deviation
4. Moisture content and loss on drying
5. Dispersion control
6. Dissolution control
7. Content uniformity
8. Microbiological controls
9. Purity check
10. Shelf-life test

Stability testing of capsules

Stability testing of capsules is performed to determine the physicochemical stability of the drug substance in the finished drug product under specified packaging and recommended storage conditions. On the intrinsic stability of the active drug molecule and the influence of environmental factors (e.g., temperature, humidity, light), formulation components and container and closure system. A battery of stress testing, long-term stability, and accelerated stability tests help determine appropriate storage conditions and expected shelf life of the product.

Material and Method

Chia seed soft gelatin capsule forms of 2 different brands and chia seed oil forms of 2 different brands, produced by various companies and offered for sale in pharmacies, were obtained from the market for use in experimental research (Desteque Chia Seed Oil Soft Capsule, Zade Vital Chia Seed Oil Soft Capsule, Naturoil Chia Seed Oil, Zade Vital Chia Seed Oil). Other materials and devices required for the tests were used from Mersin University Faculty of Pharmacy Pharmaceutical Technology laboratories.

Pharmaceutical Efficacy and Quality Control Tests

Determination of Organoleptic Properties in Soft Gelatin Capsules

At least 20 capsules were unpacked and examined. It should be smooth and without damage. Evidence of physical instability is indicated by major changes in physical appearance, such as hardening or softening, cracking, swelling, mottling, or discoloration of the shell.

Weight Deviation

This process determines the bad qualities of the filled substance, malfunctions in the operation of the filling machines or whether the controls were carried out properly during the manufacturing phase. From chia seed oil soft gelatin capsules, 10 capsules from each sample were weighed (Adventurer-O'haus, China) individually and their weights were determined. Using a suitable clean and dry cutting material, the capsules were cut and the contents were removed by washing with a suitable solvent. It was left at room temperature for 30 minutes, protected from moisture, to allow the remaining solvent in the capsule to evaporate. Each capsule was weighed individually when empty, and the net mass of the contents was calculated for each capsule by subtracting the mass of the empty capsule from the corresponding gross mass.

Dispersion Test

Disintegration studies were carried out in the PharmaTest (Germany) disintegration device in water, artificial stomach and artificial intestine medium with constant stirring (100 rpm) to determine the disintegration time. While preparing the artificial stomach and basal medium, USP XXXVI was taken as basis (13). The temperature of the water was brought to 37°C. Dispersion times in water were calculated separately using 6 capsules from all samples.

DPPH Antioxidant Capacity Measurement

It is based on determining the purple color of the DPPH (1,1-diphenyl-2picrylhydrazyl) radical, which is a free radical, by being captured by the antioxidant substance and measured in a spectrophotometer. The purple color of the radical indicates the presence of antioxidant capacity. The decrease in the absorbance of the reaction mixture indicates that the free radical scavenging activity is high.

1 ml of each of the methanolic (Merck, Germany) extracts obtained from different commercially available chia capsules was taken and 4 ml of 0.1 mM DPPH (in methanol; DPPH obtained Sigma-Aldrich, Germany) solution was added. The mixture was left in the dark and at room conditions for 30 minutes. Then, 517nm absorbance values were read on the spectrophotometer (Spectro 22-Labomed Inc., Germany). The experiment was repeated 3 times and the arithmetic averages were taken. The % DPPH radical scavenging activity was calculated by the formula below.

$$\text{DPPH radical scavenging activity (\%)} = \left(1 - \frac{\text{Absorbance of oil at 517nm}}{\text{Absorbance of control at 517nm}}\right) \times 100$$

Determination of Phenolic Substance

Methanol obtained from different chia capsules Phenolic substances in the extracts were determined by Folin-Ciocalteu reagent (FCR). In this method, phenolic compounds and Folin-Ciocalteu reagent form compounds with blue green colors. 1ml of each extract prepared from different commercially available chia capsules was taken and 45ml of distilled water (Milipor, USA; obtained and used daily in the laboratory with the device) was added. Then 1ml FCR (Sigma-Aldrich, Germany) was added. 3ml 2% after 3 minutes 100 ml of Na_2CO3 (Merck, Germany) solution was added and kept in the magnetic stirrer (Velp Scientifica, Germany) at room conditions for 2 hours. Then, absorbance values were read at 760nm on the spectrophotometer (Spectro 22-Labomed Inc., Germany). The experiment was repeated 3 times.

Results

Pharmaceutical Efficacy and Quality Control Tests

Determination of Organoleptic Properties in Soft Gelatin Capsules

Chia seed soft gelatin capsules of 2 different brands, produced by various companies and sold in pharmacies that we used in our study, are shown in Table 1.

Table 1. Determination of Organoleptic Properties of Chia seed capsules

Characteristic	A Capsule Sample	B Capsule Sample
Shapes of capsules	Oval	Oval
cover of capsules	Elastic	Elastic
	normal softness	normal softness
color	Colorless	Colorless
Dimension	Middle	Big
Smell	Odorless	Odorless

Weight Deviation

As explained in material method section, before each sample, 10 filled capsules were weighed separately with a precision balance, the capsules were emptied and the weighing process was repeated for each empty capsule. A total of 20 capsules were weighed full and empty. The results were written in the table and the standard deviation value was calculated (Tables 2, 3, values are given in grams).

Table 2. A Capsule Standard Deviation Table for Sample

Order No.	Definition	Full Capsule	Empty Capsule	Content (fat) weight	Content (fat) Average Weight	Content (fat) Standard Deflection	Content (fat) Standard Deviation %
one	weighing	0.744	0.268	0.476	0.4554	0.006866	1.44243
2	weighing	0.747	0.312	0.435	0.4554	0.0068	1.56321
3	weighing	0.729	0.250	0.479	0.4554	0.007866	1.642171
4	weighing	0.727	0.263	0.464	0.4554	0.002866	0.617672
5	weighing	0.748	0.282	0.466	0.4554	0.003533	0.758154
6	weighing	0.737	0.270	0.467	0.4554	0.003866	0.827837
7	weighing	0.736	0.278	0.458	0.4554	0.000866	0.189082
8	weighing	0.681	0.265	0.416	0.4554	0.013133	3.156971
9	weighing	0.747	0.276	0.471	0.4554	0.0052	1.104033
10	weighing	0.687	0.265	0.422	0.4554	0.011133	2.638151
					Average Standard Deflection	0.006219	

Table 3. B Capsule Standard Deviation Table for Sample

Order No.	Definition	Full Capsule	Empty Capsule	Content (fat) weight	Content (fat) Average Weight	Content (fat) Standard Deflection	Content (fat) Standard Deviation %
one	weighing	1,282	0.328	0.954	0.9373	0.0175052	1.83492
2	weighing	1,295	0.351	0.944	0.9373	0.0070974	1.177032
3	weighing	1,272	0.345	0.927	0.9373	0.0111111	1.111111
4	weighing	1,313	0.376	0.937	0.9373	0.0003218	0.034343
5	weighing	1,304	0.372	0.932	0.9373	0.0056866	0.610150
6	weighing	1,305	0.366	0.939	0.9373	0.0018104	0.192800
7	weighing	1,298	0.347	0.951	0.9373	0.0144058	1.514805
8	weighing	1,284	0.336	0.948	0.9373	0.0112869	1.190601
9	weighing	1,278	0.373	0.905	0.9373	0.0356906	3.943712
10	weighing	1,316	0.380	0.936	0.9373	0.0013888	0.148376
					Average Standard Deflection	0.0106304	

Table 4. Mean Standard Deviation Comparison

Sample (Capsule)	Average Standard Deflection
A.	0.006219
B.	0.0106304

Dispersion Test

The results of the dispersion test applied to the capsules with a disintegration device in pure water at 37±2°C are shown in the table below (Table 5). Our sample capsules were dispersed in pure water between 16 minutes 02 seconds and 18 minutes 30 seconds.

According to the results of the dispersion test applied to the capsules in an artificial stomach medium prepared according to the pharmacopoeia with a disintegration device, at a temperature of 37±2°C, the capsules dispersed between 5 minutes 14 seconds and 6 minutes 32 seconds (Table 5).

According to the results of the dispersion test applied to the capsules in the artificial intestine medium prepared according to the pharmacopoeia with a disintegration device, at a temperature of 37±2°C, the capsules dispersed between 4 minutes 49 seconds and 5 minutes 21 seconds (Table 5).

Table 5. Dispersion Rate of Capsules

Sample (Capsule)	Dispersion in Pure Water	Dispersion in Artificial Stomach Medium	Dispersion in Artificial Intestine Medium
A	16 min 02 sec	5 min 14 sec	4 min 49 sec
B	18 min 30 sec	6 min 32 sec	5 min 21 sec

DPPH Antioxidant Capacity Measurement

In the DPPH (2,2-diphenyl-1-picrylhydrazyl) free radical scavenging method, DPPH, a stable and synthetic radical, is used and antioxidant activity is defined by measuring the antioxidant's ability to capture this free radical. DPPH is a dark purple radical. It accepts a proton from the antioxidant and turns into the colorless α,α - diphenyl -β- picrylhydrazyl molecule. Its color lightens as a result of its reduction by the antioxidant substance. Its absorbance is measured at 517nm in a spectrophotometer. In this study, commercially available Chia seed oil and oil capsules were mixed with methanol. The working solutions we prepared from the extracts were mixed with DPPH solution and the absorbance values were measured on a spectrophotometer at 517nm. The methanol and DPPH solution in which the sample was dissolved was used as a blank. Butylated hydroxytoluene (BHT) was used as the standard in this study. The highest DPPH radical scavenging activity was calculated in the A capsule sample (79.49%) and the lowest DPPH radical scavenging activity was calculated in the D oil sample (41.96%) compared to the standard (Table 6).

Table 6. Chia seed oils extracts And DPPH Removal of capsules activity

Sample	% DPPH removal activity (inhibition)
A (Capsule)	79.49±1.15
B (Capsule)	74.50±4.04
C (Oil)	48.51±2.15
D (Fat)	41.96±3.87

Determination of Total Phenolic Substances

Total phenolic substances in methanolic extracts of commercially available Chia seed oils and capsules were determined by Folin Ciocalteu Reagent (FCR).

If there is a phenolic substance in the extract, the maximum absorbance value is observed at 760nm in the spectrophotometer.

The absorbance value is directly proportional to the amount of phenolic substance in the extract. Therefore, a standard gallic acid chart was prepared using gallic acid. Folin Data regarding the total amount of phenolic substances in the analysis performed according to the Ciocalteu method are shown in Table 7. The highest value was found to be 93.3 in the D oil sample, and the lowest value was 28.67 in the A capsule sample.

Table 7. Chia seed oils extracts and of capsules phenolic article amounts

Sample	Total phenolic article amount (µg GAE/mg)
A (Capsule)	27.69±2.11
B (Capsule)	36.94 ±1.85
C (Oil)	76.19 ±2.01
D (Fat)	84.26 ±1.99

Discussion and Conclusion

Due to the increase in the consumption of products of natural origin and their frequent use in the preparation of food additives, various cosmetics and pharmaceutical preparations, many plant species of medicinal and aromatic importance have gained a significant share in the world market, which is constantly increasing. In addition, due to the risk of drugs and chemicals used to protect animal and human health, many studies conducted in the fields of human and veterinary medicine, food and environment encourage the use of herbal products both in the treatment of diseases and in preventive medicine [1]. The use of nutritional products (nutraceuticals), known as alternative treatments, is increasing in every field of medicine today.

Nutraceuticals are foods or food compounds that provide health benefits as well as basic nutrition. These products are typically available in forms such as tablets and capsules. Nutraceuticals are non-toxic food supplements whose benefits have been scientifically proven in the treatment or prevention of diseases.

Today, a market worth 40-50 billion dollars has been created in the world with a wide range of products. It is the fastest growing sector, especially in the USA [2]. The leading deadly diseases seen in developed countries are cancer, cardiovascular diseases, obesity and diabetes. The increased incidence of these diseases has increased people's tendency to consume foods rich in functional nutritional components such as dietary fiber, n-3 fatty acids, antioxidants and proteins.

Chia seeds (*Salvia hispanica L.*) is the seed of the chia plant, which is a member of the mint family and belongs to the Lamiaceae family. Chia seeds are rich in oil, protein, dietary fiber, minerals and phenolic compounds. Chia seeds (100 g) contain 16 - 20 g protein, 30 - 38 g fat, 18 - 20 g n-3 fatty acids, 34 - 40 g total dietary fiber [3]. Phenolic compounds such as chlorogenic acid, caffeic acid, myricetin, quercetin, campferol and tocopherol, phytosterol and carotenoids found in chia seeds can have antioxidant effects. Chia seeds may have a protective effect against cardiovascular diseases, hypertension, inflammatory diseases and some types of cancer due to their polyunsaturated fatty acids and especially omega-3 fatty acid content [4]. Chia seeds can be added to many foods such as yoghurt and cake, either plain or by grinding them into flour and separating the oil. It can also be used as a water retainer, emulsifying agent and thickener in the food industry. Today, chia seeds are considered a functional food as a result of increasing research on their nutritional content and health effects. Chia seeds are also defined as a "super food" because they contain functional nutritional components that can be effective in preventing cancer, diabetes, obesity and cardiovascular diseases, which are common in the world in recent years [5-7].

In this study, it was aimed to determine the effectiveness and safety of chia seed (*Salvia hispanica L.*) oil and soft capsule preparations containing this oil, marketed by different companies in the Turkish market, by performing quality control tests for safe use.

Chia seeds, which contain high amounts of omega-3, on lowering cholesterol [14], fighting diabetes [15], and fighting cancer [16] have been the subject of scientific research. The n-6/n-3 ratio in chia seeds, which is a rich source of unsaturated fatty acids, was found to be 0.29. A low n-6/n-3 fatty acid ratio has been associated with a reduced risk of cardiovascular diseases [17]. Taking chia seeds; It has been reported to significantly reduce serum triglycerides and low-density lipoprotein (LDL) value and increase high-density lipoprotein (HDL) value [14]. It has also been reported that chia seeds increase the feeling of fullness and immunity, and reduce the risk of diseases such as cardiovascular and diabetes [18-19]. In another similar study, it was determined that polyunsaturated fatty acid levels (especially ALA and EPA values) increased in women who consumed 25 g of chia seeds daily for 7 weeks [20]. It was determined that body weight, triglyceride and blood sugar levels decreased by drinking 235 kcal drinks containing nopal, chia seeds, soy protein and oats at regular intervals for 2 months [21]. Tavares et al. They determined that 35 g of chia flour daily provided a 13% decrease in people's total cholesterol and a 25% increase in HDL values, and there was also a significant decrease in people's weight and waist area [24]. Azeem et al. They determined that chia seed extract increased the shelf life of cottonseed oil and significantly inhibited lipid peroxidation [24-25].

In experiments conducted on mice and humans, chia seeds reduce vision problems and kidney failure, which are the main complaints of Type-2 diabetes [26-28]. Due to the effects of functional components such as dietary fiber, antioxidants and omega-3 fatty acids contained in chia seeds, it has been observed that when consumed regularly, it protects the body against cancer and reduces the total tumor weight in an individual with cancer [29]. In a study conducted on hypertension patients; It has been observed that consumption of chia seed flour reduces blood pressure [30]. Chia seeds do not contain gluten, which is an allergenic protein. Therefore, it is suitable for consumption by celiac patients. In a study where chia seed flour was used to make gluten-free bread, it was reported that bread made from chia seeds was accepted in sensory tests and gave structurally better results than bread without chia seeds [29].

Chia seeds contain antioxidant components such as some phenolic compounds, tocopherol, carotenoids, vitamins and some peptides. Flavonoids and tocopherol are the basic structures responsible for the antioxidant capacity of the seed. The antioxidant capacity of chia seeds is 84/g, and this value is close to the antioxidant capacity of blueberries (96/g) [31]. The high antioxidant capacity allows the seed to be stored for a long time. Tocopherols are in similar amounts in chia seeds (238-427 mg/kg) and peanut oil (398.6 mg/kg) and are the most important antioxidant compounds in chia seeds. Chia seeds also contain phenolic compounds such as gallic acid, caffeic acid, chlorogenic acid, rosmarinic acid, myristin, quercetin and campferol [10]. These phenolic compounds, which can have antioxidant effects, can protect against chronic diseases such as cardiovascular diseases, diabetes and cancer by supporting the oxidative balance in the cell. Caffeic acid, chlorogenic acid and quercetin can show antioxidant properties by preventing the fats, proteins and DNA in the cell from being oxidized by free radicals [10,31].

Studies evaluating the antioxidant capacity of chia in vivo are very limited. In a study on obese rats; When chia seeds and chia oil were given to rats along with a high-fat and high-fructose diet for 6 and 12 weeks, chia seeds and oil increased catalase (CAT), glutathione peroxidase (GPx) activity in the blood, and glutathione reductase (GRd) activity in the liver. It was determined that antioxidant capacity increased by 35% and 47%, respectively [32].

Clinical studies have determined that consumption of chia seeds can provide metabolic control of type 2 diabetes and cardiovascular diseases, as well as weight loss in obesity, due to the nutritional content of the seed. Chia seeds are a natural source of n-3 fatty acids and reduce blood triglyceride [33] and β-sterol content, it can be effective in regulating blood cholesterol levels [34].

Chia seed consumption on cardiovascular diseases in humans; It was concluded that the improving effect of chia seeds on cardiovascular risk parameters is not clear [35]. However, dyslipidemic Studies on rats have shown a positive effect on the improvement of blood lipid profile. In a study conducted on dyslipidemic and insulin resistant rats; Along with a high-sucrose diet, one group was given chia seeds and the other group was given corn starch, and after three weeks, it was determined that chia seeds reduced the risk of dyslipidemia. At the end of two months, while seed consumption did not have an effect on insulin levels, it had a positive effect on dyslipidemia and reduced abdominal obesity [36]. In another study in rats Chia consumption reduced blood TG levels and helped increase HDL levels. In particular, whole chia seeds were more effective in reducing blood TG than

ground chia seeds and chia oil. Ground chia seeds significantly increased the increase of HDL compared to others [37].

In a study conducted with overweight and obese individuals with type 2 diabetes, daily consumption of 30 g/1000 kcal of chia seeds along with an energy-restricted diet helped in weight loss, improvement in postprandial glycemia, and reduction in blood CRP level [38-39].

A-linolenic acid plays an important role in the formation of some vital biochemical compounds such as leukotrienes and thromboxanes, which are linked to numerous physiological functions in the human body [40]. Additionally, ω-3 fatty acid has the ability to block calcium and sodium channel dysfunctions (which can cause hypertension), improve parasympathetic tone, and protect ventricular arrhythmia. Adding chia seeds to the diet during pregnancy helps develop the retina and brain of the fetus. The inclusion of dietary fiber and α-linolenic fatty acids in the diet makes Salba-chia a major contender in regulating body weight and possibly other comorbidities associated with diabetes [40].

Vuksan et al. showed that supplementation of 37 g/day Salba-chia into an isocaloric diet improved major and emerging risk factors in type 2 diabetes, demonstrating its cardioprotective potential while maintaining weight. A subsequent study by the same group showed that Salba-chia acutely reduces postprandial glycemia and prolongs satiety when added to a meal [38-39].

The results of studies on male Wistar rats revealed that chia seeds in the diet have a major lowering effect on triglycerides and increase beneficial HDL cholesterol. In addition, feeding chia seeds resulted in a reduction of omega6 in plasma, which consequently resulted in a lower ω-6:ω-3 ratio and subsequently had a cardioprotective effect [41].

Other studies have been conducted to investigate therapeutic effects, showing that chia seeds are a potential source of various bioactive peptides essential for the repair of damaged tissue and general well-being, as well as the control of dyslipidemia [42-43].

There are also many studies showings that chia seeds are anti-inflammatory agents, antiplatelets, anticarcinogenic, laxative, hypotensive, cardiac tonic, cardiovascular protective, analgesic, antidepressant, vision-immunity enhancer, and EPA-DHA enhancer in the blood [44-47].

In recent years, supportive treatment options have become increasingly important in the field of medicine. Chia seeds are one of the most natural products and are biologically healthy. It is a product that contains many active compounds. In light of the studies in the literature, Chia seeds are thought to be a promising treatment option as a natural product. However, its use is limited due to the lack of standardization and sufficient pharmacokinetic-pharmacodynamic studies. For a substance to be a drug, it has three basic properties: It should be targeted, its effect should be dose dependent and its effect should be temporary. Therefore, in order to use chia seeds more effectively and safely, there is a need to conduct new studies at the molecular level that can elucidate their mechanisms of action. The inadequacy of modern medicine in pathological situations such as antibiotic resistance, antineoplastic resistance, and correction of impaired homeostasis makes it important to research new drugs and treatment supports.

There are a limited number of studies on the *in vitro* and *in vivo* clinical bioactivity and safety evaluation of chia seeds, which are known to have many health benefits. On the other hand, studies have shown that chia seeds are a good source of protein, dietary fiber and unsaturated fatty acids. Chia seeds have properties such as gel former, emulsifier and stabilizer in foods, and with their high omega-3 and omega-6 content, they are an important source of enriching foods in terms of functionality. From this perspective, it is thought that chia seeds may be an important adjunctive treatment option after further studies and standardization processes.

Market preparations containing chia seed (*Salvia hispanica L.*) oil are available on the market in our country with the permission of the Ministry of Agriculture. Therefore, these preparations are not subjected to various *in vivo* and *in vitro* quality control and safety tests like other human drugs. Various problems brought about by this situation may cause the expected effect of the preparation not to be realized sufficiently. In this thesis study, antioxidant activity was determined by performing quality control tests on these products on the market.

In this study, pharmaceutical efficacy and quality control tests were conducted on chia oil and capsules provided by different companies. Despite various epidemiological and experimental reports supporting the medicinal use of chia (oral supplements), protocols regarding extraction and effective dosage must be standardized to suit human consumption on a large scale, supported by sound scientific data. The presence of chia in the diet provides a number of pharmacological properties, but knowledge and understanding of the bioactive and fatty acids responsible for its biological activity using mechanistic approaches in cell and mammalian models are still the main limitations for its broader therapeutic use.

Conflict of interest: The authors declare that they have no conflict of interest.

Acknowledgement: This thesis study was supported by Mersin University Scientific Research Projects Unit as project number 2021-2-TP2-4511.

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