

**ANDIJAN STATE MEDICAL INSTITUTE**

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**OBTAINING AND CLASSIFYING MEDICINAL FOOD SUPPLEMENTS  
BASED ON OLIVE AND SAFFRON**

**(monograph)**

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**Obtaining and classifying medicinal food supplements based on olive and saffron/Monograph/ Text.**

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**The monograph** provides information on the distribution of olive and saffron plants in nature, the chemical composition of olive oil and saffron stigmas, their use in folk medicine and their healing properties, and the use of “ASUK” and “ASQAND” food additives based on olives and saffron against inflammation and diabetes. The content of heavy metals, toxic elements, and beta-carotene in olive oil and saffron stigmas was studied.

The antioxidant, antiradical properties, anti-inflammatory and anti-diabetic activity of the food additives “ASUK” and “ASQAND” were tested *in vitro and in vivo* in vitro, and a new commodity code was developed for food additives under the TIF TN.

The monograph can be used by bachelor's, master's, doctoral students, and independent researchers conducting scientific work in the fields of commodity chemistry and folk medicine.

The monograph was approved by the expert council of the Andijan state medical institute on \_\_\_\_ \_\_\_\_\_ 2026, with statement No. \_\_\_\_\_ and recommended for publication.

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## ANNOTATSIYA

Ushbu monografiyada zaytun va za'faron o'simliklarining tabiatda tarqalishi, zaytun moyi va za'faron gultumshuqchalarining kimyoviy tarkibi, xalq tabobatida qo'llanilishi, zaytun moyi va za'faron gultumshuqchalarining tarkibidagi og'ir metallar, zaharli elementlar, za'faron gultumshuqchalari tarkibidagi beta-karotin miqdori aniqlanganligi, "ASUK" va "ASQAND" oziq-ovqat qo'shilmalarining antioksidantlik, antiradikallik xususiyatlari, yallig'lanish hamda qandli diabetga qarshi faolligini *in vivo* sharoitda tekshiruvdan o'tkazilganligi va bu oziq-ovqat qo'shilmalariga "Tashqi iqtisodiy faoliyat tovarlar nomenklaturasi" bo'yicha yangi tovar kod ishlab chiqilganligi ko'rib chiqilgan.

## АННОТАЦИЯ

В монографии рассматриваются вопросы распространения растений семейства оливковых и шафрановых в природе, химический состав оливкового масла и шафрановых крокусов, их применение в народной медицине, определение содержания тяжелых металлов и токсичных элементов в оливковом масле и шафрановых крокусах, содержание бета-каротина в шафрановых крокусах, испытания *in vivo* антиоксидантных, антирадикальных свойств, противовоспалительной и антидиабетической активности пищевых добавок «ASUK» и «ASQAND» и разработка нового товарного кода для этих пищевых добавок в рамках «Товарной номенклатуры внешнеэкономической деятельности».

## ANNOTATION

This monograph reviews the distribution of olive and saffron plants in nature, the chemical composition of olive oil and saffron crocuses, their use in folk medicine, the determination of heavy metals and toxic elements in olive oil and saffron crocuses, the content of beta-carotene in saffron crocuses, the *in vivo* testing of the antioxidant, antiradical properties, anti-inflammatory and anti-diabetic activity of the food additives "ASUK" and "ASQAND" and the development of a new commodity code for these food additives under the "Nomenclature of goods of foreign economic activity".

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## ABBREVIATIONS

1. WHO – World Health Organization
2. IDF – International Diabetes Federation
3. QD – Diabetes
4. TIF TN – Foreign Economic Activity Commodity Nomenclature
5. CIS – Commonwealth of Independent States
6. USA – United States of America
7. HPLC – High Performance Liquid Chromatography
8. TY – Technical Instruction
9. WHO – World Health Assembly
10. ONF – Tumor necrosis factor
11. UFA – Monounsaturated Fatty Acid
12. QTZM – Extra virgin olive oil
13. OPS - Optical emission spectrometer
14. DFPG – Diphenyl picryl hydrazyl
15. ARF – Antiradical activity
16. DMSO – Dimethyl sulfoxide
17. LPO – Lipid Peroxidation
18. NADF - Nicotinamide adenine dinucleotide phosphate
19. Hb – Hemoglobin
20. AEF – Antiexudate activity
21. EM – Exudate mass
22. EB – Exudation suppression
23. GM – Granuloma mass
24. PB – Proliferation suppression
25. KFS h – Active form of oxygen
26. TBK – thiobarbiturate acid
27. MDA – Malon dialdehyde
28. UT – Unified System
29. AD – Alloxan diabetes
30. DSt – State Standard

## **Introduction**

Determining the chemical composition of medicinal plants in the world, developing natural, harmless food additives based on them that are beneficial to the human body, and identifying their beneficial properties are considered one of the most pressing issues. In this regard, the development and use in folk medicine of natural, harmless and environmentally friendly food additives based on parts of medicinal plants from different growing seasons, which can be used as an adjuvant to synthetic drugs, contain biologically active compounds such as vitamins, flavonoids, macro- and microelements, and have the properties of treating and preventing various inflammatory diseases.

A number of studies are being conducted worldwide to develop dietary supplements made from natural biologically active compounds isolated from medicinal plants that have the properties to prevent and treat inflammation and diabetes. In this regard, special attention is being paid to the development of biologically active food additives based on medicinal plants that can replace some synthetic agents that treat or prevent inflammation and diabetes. For this reason, it is important to create food additives with the properties of treating and preventing inflammatory and diabetic diseases, based on olive oil and saffron, which contain natural compounds that have a positive effect on inflammation and normalize blood sugar levels, to determine their chemical composition and structure, and to develop new international commodity code numbers for them under the TIF TN.

Our republic is achieving certain results in the development and implementation of natural food additives that have the properties of increasing the immunity of the human body, as well as preventing and treating many diseases. The development strategy of the new Uzbekistan has identified important tasks to be implemented under the «Implementation of the Food Industry Development Program» . Based on these tasks, the creation of harmless, natural biologically active food additives based on olives and saffron that contain compounds that prevent inflammation and diabetes, increase the body's immunity, as well as the

study of their chemical composition, structure ,\_properties, and the development and implementation of commodity codes in accordance with the rules of the harmonized system are of great scientific and practical importance.

Many scientists have worked on the chemical analysis of the composition of medicinal herbs and the study of biologically active substances found in them, including their anti-inflammatory and antidiabetic properties.

In particular, in the USA, DJNewman, GMCragg , in European countries, for example, German scientist A.Helmstadter , Polish scientist M.Przeor conducted scientific research on the creation of new natural food additives based on animal and medicinal plants that have anti-inflammatory and blood sugar-lowering properties. In the CIS countries, EBArushanyan, ONDimbrilova, LALapinina, AASpasov conducted scientific research in this area, while among our scientists, Doctor of Chemical Sciences, Professor IRAskarov, along with Doctors of Philosophy in Chemical Sciences (PhD) GNMadrakhimov, NTYolchiyeva, U.Sh.Khusanov and ZOMirzayeva, many fruitful scientific researches have been conducted and are still being successfully continued today.

Currently, food additives made from olive (*Olea europaea* ) oil and saffron (*Crocus sativus* L.) flower buds have not been used in medical practice, including as anti-inflammatory agents and as a means to lower blood sugar levels in patients with diabetes, and no scientific studies have been conducted.

aims to address the problems of using food supplements based on olive and saffron plants to treat various inflammatory diseases and as a means of lowering blood sugar levels in diabetes.

# **I. DISTRIBUTION OF SAFFRON, OLIVE AND FLAX PLANTS IN NATURE, THEIR CHEMICAL COMPOSITION AND THEIR IMPORTANCE IN FOLK MEDICINE IN THE TREATMENT OF CERTAIN DISEASES**

## **§ 1.1. The history of the science of “Folk medicine” and its importance today**

With the emergence of man on our earth, medicine also emerged naturally. Because, as long as man is alive, there is also this disease. When it comes to treatment for diseases, man has sought it from nature and turned to medicine, which is a unique product of nature, has found and continues to find it. In nature, the most favorable conditions for human health, nutrition, survival, and reproduction are embodied. Because, the Creator has appointed man as the ruler of the earth, and has made all the elements in it, living and non – living nature, and existing animals subordinate to him. This is clear evidence that for several thousand years, humanity has been preserving the health of itself and others through the rational use of natural and animal – derived healing remedies, known as folk medicine [1; p. 3].

Ibn Zakariyy, Ar- Razi, Ghafiqi, Biruni, Qurtubiy, Ali Hisraviy, Vanand Dinawariy, Abul-Qasim Zahrawiy, Abul-Tussin Jaridiyy, Abul-Faraj Abdullah ibn Tayyib, Abul-Hasan Addamashqiyy, Abbas Majusiyyy, At-Tabariyy, Amirdawlat Amasiatsiyy, Abu Ali ibn Sinoyyyy and other scholars of medicine proposed various phytotherapeutic methods for treating patients [2; p. 8].

In the history of folk medicine, the place of Muhammad’s medical recommendations and advice is incomparable, and this is an invaluable The teachings are collected by the scholars of hadith in the form of hadiths and are widely used in the form of a treatise called “Tibbi Nabiy” (“Medicine of the Prophet” ) [3; pp. 5-6].

Population of many countries of the world has made its due contribution to the development of folk medicine, and this process continues. In particular, folk medicine has been used by the Chinese since ancient times. Although animal and

mineral materials are used in it, plants are considered the main source of medicines. There are about 5,000 folk medicine methods in China, which account for about one fifth of the entire Chinese pharmaceutical market [4; pp. 7-8].

Ayurveda is a medical system that originated in India and has been in use for nearly 5,000 years. It focuses on the body, mind, and spirit in the prevention and treatment of disease, and involves the use of diet and herbal remedies [5;].

The desire to benefit from the wisdom of traditional medicine systems has led to a resurgence of interest in herbal medicines in Europe and North America. Consumers have been positive about these products, believing that they are safer than synthetic products because of their natural origin and that they are part of a healthy lifestyle [6; pp. 447-452].

Traditional medicine, known as “Traditional Medicine” or “Complementary and Alternative Medicine” is gaining international recognition and increasing importance. In order to further strengthen traditional medicine and its role in maintaining the health of the world’s population, the World Health Organization has developed a separate strategy for 2014-2023, which will strengthen the role of traditional medicine in maintaining the health of the population. [7;].

In our country, folk medicine has very deep roots, and there are certain signs that people used folk medicine methods several thousand years ago. In 1926, the former Soviets put an end to folk medicine. During this period, doctors and folk medicine specialists worked secretly. They preserved the traditional methods of treatment inherited from their ancestors from generation to generation as a treasure trove [2; pp. 9-10].

Today, our government is implementing major reforms to restore the status of the traditional medicine sector and further develop it. In particular, the Resolution of the President of the Republic of Uzbekistan dated October 12, 2018 No. PQ - 3968-n “On measures to regulate the sphere of folk medicine in the Republic of Uzbekistan”, the Decree of the President of the Republic of Uzbekistan dated May 20, 2022 No. PF - 139 - n “ On measures to promote the effective use of the raw material base of medicinal plants, support their processing,

and create an added value chain through it” and the Decree of the President of the Republic of Uzbekistan dated May 20, 2022 No. PF-139- n “On measures to organize the cultivation and processing of medicinal plants in a cultural state and their widespread use in treatment” The adoption of Resolution No. PQ -251-s “On” has paved the way for the development of the field of folk medicine, as well as for the activities of folk medicine specialists [8; p. 3].

In 2019, the science of folk medicine was proposed as the 41st science in the world system of medical sciences by the Chairman of the Academy of Medicine of Uzbekistan, an inventor who served in Uzbekistan, Doctor of Chemical Sciences, Professor Askarov Ibrahim Rakhmonovich, and the full member of the Academy of Medicine of Uzbekistan, Doctor of Medical Sciences, Professor Nematjon Soliyevich Mamasoliyev. After the relevant studies, this science was officially registered by the Higher Attestation Commission under the Cabinet of Ministers of the Republic of Uzbekistan as a specialty “14.00.41 – Folk Medicine” . As a result, for the first time in the world, the specialty of Folk Medicine was created in Uzbekistan. [2; p. 3].

Over the past years, a number of researchers have conducted scientific research in the field of folk medicine and received the degrees of Doctor of Science and Doctor of Philosophy. In particular, scientists such as Mominjonov Mirjalol Mukimjonoglu, Mamatova Irodakhan Yusupovna, Isayev Yusufjon Tojimamatovich, Abdulloyev Obidjon Shakhbiddinovich, Kholboyev Yusufjon Khakimovich and Ismoilov Akmal Khushvakovich received the degrees of Doctor of Science (Dsc), and scientists such as Abdulloyev Murodjon Nemadjonovich, Razzakov Nabidjon Alijonovich received the degrees of Doctor of Philosophy (PhD). Many researchers continue to conduct scientific research in the field of folk medicine [8; pp. 4-5].

It can be said with confidence that folk medicine has been improving and tested over the centuries, but at the same time it has not lost its importance. Today, the state support for its development in our country and its recognition as a science

encourages researchers to contribute to the development of science and further improve it.

## **§ 1.2. The role of food additives in human health**

With the world population now approaching 8 billion, the significant increase in the incidence of various diseases, such as cardiovascular diseases, cancer, diabetes, and chronic respiratory diseases, and the increase in deaths from various diseases, necessitates a global focus on their prevention and treatment in all regions of the world, as well as on the fight against injuries. In particular, the number of deaths from heart disease has increased from 2 million to nearly 9 million per year in the last 20 years, accounting for 16% of all deaths. Deaths from diabetes have increased by 70% worldwide [9;].

This and different diseases prevent to take and in treatment used medicine to their products happened of need increasingly increasing progress medicine of products shortage gone For example, only half of the 100 million people in the world who need insulin have access to it reliably [10; pp. 180-182].

Another aspect of the issue should not be overlooked, namely the adverse reactions of synthetic drugs. For example, Amidopyrine (for inflammation) can cause disorders of white blood cells, clioquinol (for skin infections) can cause vision disorders, erythromycin (antibacterial) can cause hepatitis (liver disorders), oral contraceptives can cause thromboembolism (blood clotting), statins (for cholesterol control) can cause muscle degeneration, and thalidomide (for the treatment of morning sickness) can cause phocomelia (body deformity in infants) [11;].

In the United States, approximately 8% of hospital admissions are due to adverse or side effects of synthetic drugs. Synthetic drugs cause approximately 100,000 deaths each year. Deaths or hospitalizations due to herbal medicines are very rare [12; pp. 40-44].

Herbal medicines can be used as a treatment for sleep, stress, digestive disorders, colds and flu. Herbal medicines are also used to treat many diseases,

such as asthma, eczema, rheumatoid arthritis, migraine, chronic fatigue, inflammatory bowel syndrome and cancer [13; pp. 1408-1411].

Herbal therapy is a holistic therapy that integrates emotional, mental, and spiritual levels. Of course, when using medicinal plants, it is necessary to have sufficient knowledge about their effects on the human body and to follow the necessary instructions [14; pp. 13-14].

According to the World Health Organization, up to 80% of the population in some Asian and African countries currently use herbal medicines for primary health care. Approximately 25% of modern medicines used in the United States are derived from plants [15; p. 69].

Current estimates suggest that a large proportion of the population in many developing countries relies heavily on traditional practitioners and medicinal plants to meet their primary health care needs. The World Health Organization (WHO) estimates that the global market for herbal medicines and herbal products is worth US\$62 billion and is expected to reach US\$5 trillion by 2050 [16; p. 154].

Today, the industrial production of various medicinal products from herbal substances is an important issue, and the WHO Good Manufacturing Practices for Herbal Medicines (GMP) developed separate guidelines on good manufacturing practices [17;].

As in many countries of the world, special attention is paid to the preparation of medicinal products, ointments, tinctures and food additives from plants in our country. In particular, the chairman of the Academy of Medicine of Uzbekistan, Honored Inventor of Uzbekistan, Doctor of Chemical Sciences, Professor Askarov Ibrohim Rakhmonovich, created the food additives “Majmui Rahmaniy”, “Askalisiy”, “Shifoi Marhaboxon”, “Oltin Vodiy”, “Asshifo”, “Asdavo” . Also, Professor Askarov and a number of scientists jointly created the first in the world new natural food additives “AS-CURCUMIN”, “ANTICOVIR”, “ANTIVIR 101”, “ASKAROVIR” that prevent viral diseases [2; p. 4].

Based on the above information, it can be concluded that, although the use of synthetic agents in the treatment of diabetes and inflammatory diseases is

effective, their negative side effects necessitate the search for alternative, harmless natural agents.

### **§ 1.3. Problems of classifying food additives according to the Foreign Trade Classification System**

Today, there are 20 disciplines within the chemical sciences, which were discovered in 10 countries around the world. The emergence of each discipline is a unique global event. Because they were discovered at a time when the methods of existing sciences were insufficient to solve the scientific, social, economic and other problems of their time [18; pp. 14-15].

For example, organic chemistry emerged as a science that was supposed to solve problems aimed at determining the composition, structure, properties, and transformations of compounds formed in living nature, at a time when the chemical components of organic substances were still unknown [19; p. 5].

Another important science, biochemistry, emerged as a science that combines various methods of chemistry, physics, and molecular biology to explain the mysterious functioning of the organism, helps explain the causes of diseases in medicine, and as a result, offers adequate methods of treatment and diagnosis, identifies a number of physiological and pathological aspects, and studies various healthy and pathological conditions [20; pp. 63-74].

Due to the historical necessity of solving many problems in foreign economic activity, in 1997 a new discipline, “Classification and certification of goods based on their chemical composition”, was discovered in Uzbekistan by the honored inventor and rationalizer IRAskarov and the Doctor of Technical Sciences, Academician TTRriskiyev. The discipline was assigned the specialty code 02.00.22 [21; p. 10].

In this specialty, it is planned to conduct economic research, along with chemical and technological research, such as studying the composition, extraction, origin, structure, organoleptic and physicochemical parameters of substances in

connection with the description and certification of goods according to the TIF TN [22; p. 529].

In 2017, the inventor and rationalizer, PhD, Professor IRAskarov, who served in Uzbekistan, proposed a new name for the science as “Commodity Chemistry” and a science passport, which was approved by the UAC and given the code 02.00.09 - Chemistry of Goods. Due to the practical application of the new science, the correct assignment of international code numbers to goods based on their chemical composition is bringing great economic benefits, and billions of material losses that could be caused to the treasury of our Republic due to the incorrect assignment of code numbers to goods are being prevented [23; p. 7-9].

Commodity chemistry is a young, rapidly developing science. It can be said that this science is used to apply scientific innovations in the field of chemistry to practice, production and various sectors of the national economy, to accurately and quickly implement import-export processes. Assigning code numbers to existing and new goods according to their chemical composition plays a decisive role in protecting public health and economically [24; pp. 38-41].

The use of medicinal, safe food supplements made from natural products is invaluable in improving human health and treating various diseases, and it is an important task to classify such products based on their chemical composition and assign them an appropriate commodity code.

Today, the above task is being accomplished by a number of researchers and scientists, effectively using the methods of commodity chemistry.

In particular, Doctor of Philosophy (PhD) in Chemistry NARazzakov classified the natural food additives “ VITOON” and “KALMAVIT” under subheading 121230 of the TIF TN - “Food additives made from medicinal plants or their parts” and assigned them: “Natural food additives containing marigold and cinquefoil” - 121230000 5 international commodity code numbers, which are currently being used in customs practice [25; p. 101 ].

Also, Doctor of Chemical Sciences (DSc) MMM O’minjonov developed the international commodity code numbers for the natural food additives “Asdavo”

and “Alkaman” under the subheading 121230 of the TIF TN – “Food additives prepared from medicinal plants or their parts”, and assigned them: “Natural food additives prepared on the basis of melon seeds and peel, oat bran, dalacoy and jambil roots” - 1212300003, “natural food additives prepared on the basis of nut fruit waste, enriched with certain medicinal plant parts” - 1212300004, which is now being used in customs practice [26; ].

The use of medicinal, safe food additives made from plants is invaluable, and classifying such products based on their chemical composition and assigning them the appropriate commodity code under the TIF TN is an important task.

#### **§ 1.4. Distribution, chemical composition and medicinal properties of the saffron plant in nature**

Saffron (*Crocus sativus* L.) is a perennial herb belonging to the Iridaceae family. It flowers in February and bears fruit in April-August. Wild species grow in the hills and mountains of Tashkent and the Fergana Valley [3; p. 379].

Saffron is a bulbous plant that can reach a height of 30 cm, has long and thin leaves, and purple flowers. Saffron reproduces vegetatively. The number of flowers reaches 4-12. Each flower has three yellow stamens, which hold three red-orange stamens that emit a strong aromatic scent. The diameter of the bulb is 4.5-5.5 cm [27; pp. 234-242].

Saffron has been cultivated in the Mediterranean region since the late Bronze Age. Its long, crimson florets were prized for their aromatic flavor and golden-yellow color. They were also used to dye textiles [28; pp. 19-23].

Some scholars suggest that saffron originated and was domesticated in the Near East, while others suggest Central Asia or the southwestern Greek islands. From this main area, it spread to India, China, and the Middle East, from where the Arabs spread it throughout the Mediterranean basin, including Morocco [29;].

Saffron is cultivated in many countries around the world today. Although Iran is the leading country, it is also cultivated on a smaller scale in Greece, India, Azerbaijan, France, Italy, Austria, Belgium, Germany, the Netherlands, Spain,

Hungary, China, Japan, Norway, Russia, Morocco, Turkey, Israel, Egypt, the United Arab Emirates, Mexico, Switzerland, Algeria, Australia, and New Zealand [30; pp. 426-432].

The total amount of saffron produced worldwide is approximately 475 tons per year. Today, Iran, which accounts for more than 85% of the world's saffron production, is the world's leading saffron producer with an area of 115,000 ha and an annual production of 405 tons. India (22 tons, 4.6%) and Greece (7 tons, 1.5%) are next. Morocco is the world's fourth largest producer with a production of 6.8 tons in 2018 on an area of approximately 1,800 ha [31; pp. 1062-1069].

Collecting flowers and separating the stigmas is a time-consuming and labor-intensive process. Saffron flowers should be collected on the day they appear. The collection is carried out for a short time at dawn. Because under the influence of sunlight, saffron quickly loses its color and flavor and becomes faded [32; pp. 95-112].

Saffron cultivation, as it depends on many environmental, biological and anthropogenic factors. One kilogram of intact flowers yields 72 g of fresh saffron (florets), which in turn yields 12 g of dried saffron. Saffron yields are reported to average 4 to 6 kg per hectare in Iran, 8.4 and 6.5 kg in Italy and Spain, respectively, 1.57 to 3.74 kg in Kashmir under non-fertilized and rainfed conditions, 24 kg in New Zealand, and 2 to 6 kg in Morocco [33; pp. 1-28].

The saffron plant consists of a bulb, leaves, and flower organs.

The saffron flower is considered the most expensive spice in the world due to its edible, three-lobed, dried stigmas [34; p. 399].

Saffron has been identified to contain more than 150 volatile and non-volatile chemical compounds. These include a number of volatile and non-volatile active compounds that provide biological activity, such as carotenoids, anthocyanins, lycopene,  $\alpha$ - and  $\beta$ -carotene, zeaxanthin, crocetin and its derivatives. At the same time, flavonoids, vitamins (especially riboflavin and thiamine), amino acids, proteins, starch, minerals and various other chemical compounds have also

been identified in saffron. The four main and biologically active compounds in saffron are crocin, crocetin, picrocrocin and safranal [35; pp. 8-38].

The composition of saffron grown in different countries may vary. Studies have shown that the chemical composition of saffron is approximately as follows: 8-15% water, 12-15% carbohydrates, 10% tannins, 8% pentosans, 6% pectins, 6% starch, 2% crocins, 1% other carotenoids, 12% proteins and amino acids, 6% minerals, 6% non-volatile oils, 1% volatile oils and 5% miscellaneous substances [36; p. 8].

Carotenoids are the most important components of the spice and give saffron its characteristic color. They include fat-soluble compounds such as  $\alpha$ - and  $\beta$ -carotene, lycopene, and zeaxanthin, and water-soluble compounds such as the apocarotenoid crocetin and crocins, polyene esters of the mono- and di-glycosides crocetin. Crocins are water-soluble members of the carotenoid family, as they are mono- and di-glycosylated esters of the dicarboxylic acid crocetin. They constitute 3.5% of the weight of the plant stigmas [37].

Two compounds have been identified as carotenoid oxidation products: picrocrocin (a monoterpene glycoside) and safranal (a cyclic monoterpene aldehyde). Picrocrocin, which constitutes 3.7% of the weight of saffron florets, has been identified only in *the Crocus* genus, the only edible spice from which is *Crocus sativus L.*, i.e. saffron [38].

Saffron flowers contain a total of 827 chemical compounds from 35 categories, including 92 alkaloids; 42 amino acids and their derivatives; 7 anthraquinones; 16 benzene derivatives; 7 carbohydrates; 16 carboxylic acids and their derivatives; 3 cholines; 26 coumarins; 18 diterpenoids; 146 flavonoids (including flavone, flavanone, and flavonoid); 5 indole derivatives; 8 iridoids; 4 keto acids and their derivatives; 5 lipids; 14 monoterpenoids; 26 nucleotides and their derivatives; 11 organic acids; 7 organonitrogen compounds; 27 oxygenated organic compounds; 70 phenols and phenol esters; 40 phenylpropanoids; 8 phytohormones; 8 prenol lipids; 23 pteridines and derivatives, purine nucleosides, pyridines and derivatives, pyrimidine nucleosides, pyrimidine nucleotides and

pyrrolopyrimidines; 12 quinones; 38 steroids and steroid derivatives; 21 triterpenoids; 6 vitamins and 33 other compounds have been identified. 824 metabolites have been identified in the petals. 821 of them are also present in the stamens. Three metabolites (cassin, rutin and iringaresinol-di-glucoside) differ from the stamens [39; p. 2427].

Studies on saffron grown in the Torbat-e-Haydari region of Iran have revealed the presence of several metals in its various parts. The saffron corms, petals, and stigmas were analyzed (Table 1.1). [40; pp. 283-296].

Table 1.1.

Quantitative values of metals in different parts of saffron in mg/100g.

Name of metals	Root onion	Petal	Gultumshukchi
Sodium	121,467	40,733	19.88
Magnesium	349,167	353,167	187,667
Potassium	422.5	1416,667	1409.00
Calcium	697,667	315,833	475.5
Iron	325,133	92.6	47.95
Zinc	14,572	3,917	3,042

Like the stigmas of saffron, its petals have also become an object of interest to scientists due to their pharmacological properties[41;].

Studies have shown that it has antibacterial [42; pp. 69-82], antispasmodic [43; pp. 75-84], anti-depressant [44; pp. 1981-1989], anti-hypertensive and anti-diabetic effects. It also has hepatoprotective and antioxidant activity. Saffron petals grown on farms near Tehran, another region of Iran, contain biologically active organic compounds such as proteins, fats, flavonoids, carotenoids, terpenoids, as well as sodium, potassium, calcium, magnesium and other biogenic elements. Some of the elements and their amounts in saffron petals are listed below (Table 1.2.) [45; pp. 1091-1099].

Table 1.2.

Some biogenic elements in saffron petals and their amounts (mg/100g).

Item name	Sodium (Na)	Potassium (K)	Calcium (Ca)	Copper (Cu)	Iron (Fe)	Magnesium (Mg)	Zinc (Zn)	Phosphorus (P)
Amount (mg/100g)	25.75	1,542.13	486.25	0.87	17.99	293	1.8	209.9

Germany, the name saffron is derived from the Arabic word for yellow. The use of saffron dates back to ancient Egypt and Rome, where it was used as a dye, perfume, and medicine, as well as in cooking [46; pp. 39–59].

As a medicinal plant, saffron has traditionally been used as an antidepressant, respiratory aid, antispasmodic, and sedative. In folk medicine, it has been used to treat smallpox, colds, asthma, eye and heart diseases, and cancer. Saffron can also be used as a topical agent to cleanse wounds and reduce teething discomfort in infants [47; pp. 20–25].

Studies conducted in India report that consuming fifty milligrams of saffron dissolved in 100 ml of milk twice a day significantly reduced the oxidative susceptibility of lipoproteins in patients with cardiovascular disease, indicating the antioxidant potential of saffron [48; pp. 205-207].

Crocin analogues isolated from saffron have been shown to significantly increase retinal blood flow and facilitate the restoration of retinal function. The authors suggest that crocin analogues may be used to treat ischemic retinopathy and its age-related complications [49; pp. 143–152].

Trans-crocin-4, a digentibiosyl ester of crocetin, a major carotenoid, has been shown to inhibit amyloid-beta fibrillogenesis, which is the oxidation of amyloid beta-peptide fibrils in Alzheimer's disease. A water-methanol (50:50, v/v) extract of saffron crocus has been shown to inhibit amyloid-beta fibrillogenesis at lower concentrations and in a time-dependent manner than other dimethylcrocetin compounds [50; p. 8762].

In studies aimed at determining the hypolipidemic effect of saffron, crocin, one of the components of saffron, was found to have a hypolipidemic effect in diet-induced hyperlipidemic rats at doses ranging from 25 mg/kg to 100 mg/kg body weight, which is equivalent to 100 mg/kg body weight [51; pp. 116-122].

In animal experiments, aqueous and ethanolic extracts of saffron stamens and petals have been shown to have acute and chronic antinociceptive and anti-inflammatory effects, as demonstrated by the acetic acid-induced writhing test,

xylene-induced ear edema in mice, and formalin-induced edema in the rat paw. This supports its traditional use as an anti-edema agent [52; pp. 22-26].

It has been reported that the methanol extract of saffron florets and its components safranal, crocin, and other components have radical scavenging activity, which allows its use as a treatment for age-related diseases, cosmetics, food supplement, etc. [53; pp. 997-1000].

Crocetin has been shown to have greater antioxidant capacity than alpha-tocopherol in glucose-starved neuronally differentiated pheochromocytoma cells. It increases the levels of various enzymes, such as glutathione reductase and glutathione-S-transferase, and also maintains the functional levels of other antioxidants, suggesting its potential as an antioxidant [54; pp. 61-64].

Crocetin, the main active ingredient of saffron, reduces the activity of the cardiac marker lactate dehydrogenase and also increases mitochondrial potential in cardiac myocytes treated with noradrenaline, which indicates its cardioprotective effect [55; pp. 787-791].

Saffron has also been shown to have calcium antagonistic activity. This antagonistic activity was mediated by blocking extracellular Ca influx through receptor-gated Ca<sup>2+</sup> channels and voltage-gated Ca<sup>2+</sup> channels [56; pp. 151-155].

In another study, crocetin was found to prevent norepinephrine-induced cardiac hypertrophy by increasing the levels of antioxidant enzymes such as myocardial superoxide dismutase, catalase, and glutathione peroxidase, due to its potent antioxidant activity, and also significantly improve norepinephrine-induced myocardial pathological histological changes [57; pp. 348-352].

Another study aimed at determining the biological activity of crocetin revealed that it has antidiabetic activity because it attenuates free fatty acid-induced insulin insensitivity and dysregulated adiponectin mRNA expression, and also suggests that crocetin treatment may be a preventive strategy for primary NF- $\alpha$ , leptin, and insulin deficiency and related diseases [58; pp. 64-72, 59; pp. 887-898].

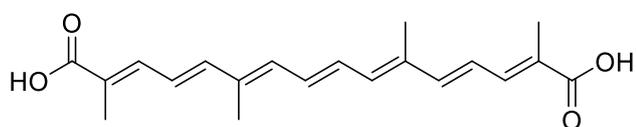
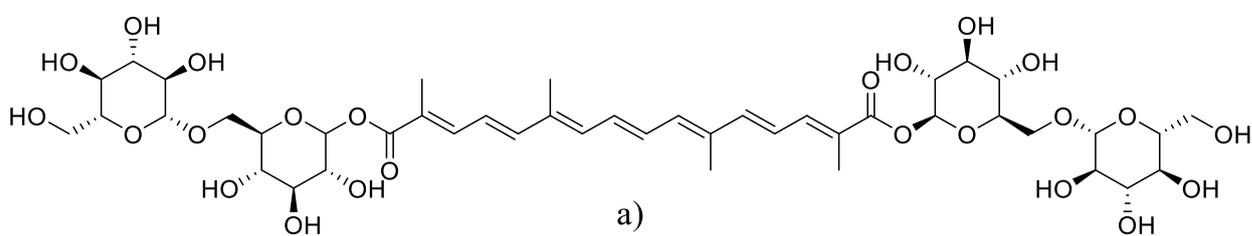
Advanced glycation end products are known to induce oxidative stress, which usually leads to endothelial cell apoptosis and therefore to diabetic vascular complications. Crocetin may be a good agent in diabetic vascular complications due to its good antioxidant capacity and calcium antagonistic activity or stabilization [60; pp. 268-274].

In scientific studies on the effects of saffron on smooth muscle, it has been shown to have a sedative effect. A sedative prepared from a water-ethanol extract and safranal was found to be more effective than saline and theophylline as controls. This suggests that saffron may be used as a sedative in the treatment of asthma and various other respiratory diseases [61; pp. 1385-1390].

In a rat model of middle cerebral artery occlusion (acute cerebral ischemia model), the decrease in the activities of superoxide dismutase,  $\text{Na}^+$ ,  $\text{K}^+$ -ATPase, catalase, and other enzymes was reversed by pretreatment of the animals with crocetin. This allows the use of saffron in focal ischemia [62; pp. 246-253].

Crocetin has shown itself to be a promising treatment for Parkinson's disease because it protects the substantia nigra in the brain from the damaging effects of 6-hydroxydopamine [63; pp. 805-813].

Behavioral and electrophysiological studies have shown that saffron extract enhances learning and memory in experimental animals. Saffron extract or its active components, crocetin and crocin, may be useful in the treatment of neurodegenerative diseases accompanied by memory impairment [64; pp. 149-152].



b)

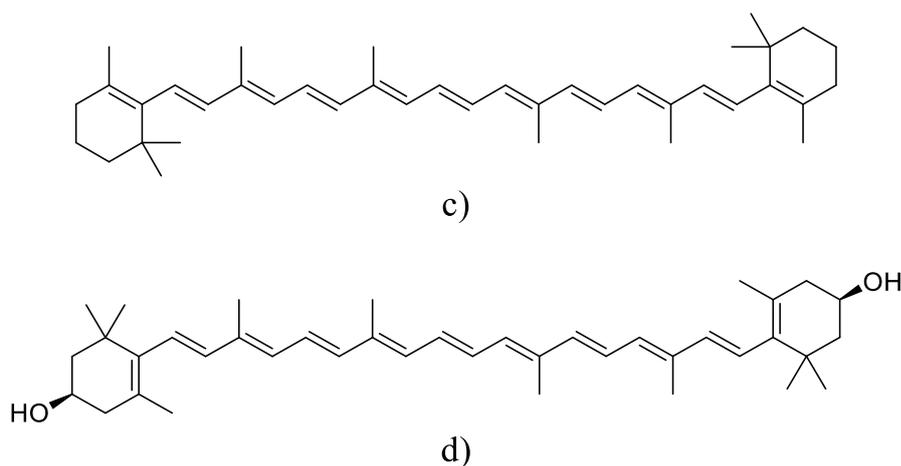


Figure 1.1. Important biologically active compounds found in saffron: a) crocin; b) crocetin; c)  $\beta$ -carotene; d) zeaxanthin.

The medicinal properties of saffron are explained by the presence of many biologically active compounds in its composition. Its beneficial effect in a number of diseases, especially its hypoglycemic properties, necessitates the development of a food supplement that can be used in the treatment of diabetes mellitus and the study of the biological properties of the resulting food supplement.

### § 1.5. Distribution, chemical composition and medicinal properties of the olive plant in nature

Olive ( *Olea europea*, *Oleum olivarum* L. ) is an evergreen tree belonging to the olive family. It is about 3-7 meters tall, with small and pointed leaves. Its flowers are white, collected in a raceme. The fruit is a drupe [3; p. 366].

It is of immense importance in the pharmaceutical, food industry, cosmetics and other fields . It is mentioned in the Quran, the Bible and the Torah as a symbol of wisdom, fertility and peace. In particular, the fact that it is mentioned seven times in the Quran itself shows how valuable the olive is. The olive also had a special place in the medicine of the Prophet. Muhammad (peace be upon him) used a mixture of olive oil and saffron to treat pleurisy [65; pp. 25-26].

Olive trees have been cultivated in the Mediterranean basin since 6500 BC and have had a significant impact on the economy, history, culture, and

environment of the region. International analyses show that olive trees are now cultivated on 11.5 million hectares in 58 countries on 5 continents [66; 79, 97].

The olive is one of the most important crops in the Mediterranean countries. Olive trees are grown in many areas around the world, 98% of which are located in the Mediterranean basin [67; pp. 16-24].

Olives have been widely studied for their nutritional uses, and their fruits and oil are an important component of the daily diet of a large portion of the world's population [68; pp. 1153-1162].

The chemical composition of olive oil consists primarily of triacylglycerols, followed by a number of compounds such as free fatty acids, mono- and diacylglycerols, hydrocarbons, sterols, aliphatic alcohols, tocopherols, and pigments[69; pp. 175-187].

The composition of olive oils can vary from sample to sample, depending on the region of cultivation, the variety, and the ripeness of the fruit. Greek, Italian, and Spanish olive oils are low in linoleic and palmitic acids and high in oleic acid. Tunisian olive oils are high in linoleic and palmitic acids and low in oleic acid [70; pp. 2113-2121].

Olive oils contain about 98-99% fatty acids, mainly in the form of triacylglycerols, 55-83% oleic acid esters, 7.5-20% palmitic acid, 3.5-21% linoleic acid and 0.5-5% stearic acid, among other fatty acids . Approximately 40% of the triacylglycerols present in olive oil are triolein [71; pp. 16-33].

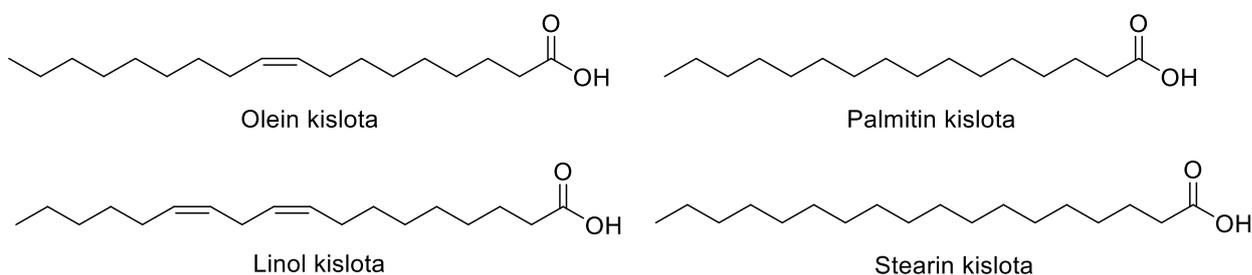


Figure 1.2. Structural formula of fatty acids in olive oil.

Olive oil also contains many other components in small amounts. These minor components are very important: some have beneficial effects on human health, others are important in increasing the stability of the oil, and still others

provide its unique aroma. Examples of minor components of olive oil include tocopherols, phenols, aromatic compounds, hydrocarbons, and sterols [72;].

Olive oil contains up to 43 mg/100 g of alpha-tocopherol, a member of the vitamin E family. One tablespoon of olive oil contains 1.9 milligrams of vitamin E, which is 10% of the daily value of a 2000-calorie diet. Obviously, the amount of these compounds present in the oil depends on several factors [73; pp. 1770-1775].

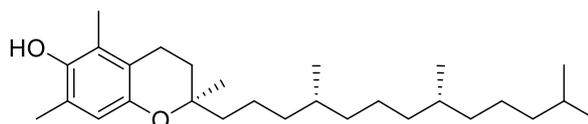


Figure 1.3. Structural formula of  $\alpha$ -tocopherol.

Olive oil contains a number of phenolic compounds, including simple phenolic compounds such as vanillic acid, gallic acid, coumaric acid, caffeic acid, tyrosol, and hydroxytyrosol. On average, 100 g of olive oil contains 4.2 mg of simple phenolic compounds. In addition, olive oil contains secoiridoids such as oleuropein and ligstroside (2.8 mg/100 g in extra-refined oil and 0.93 mg/100 g in refined oil, respectively) or lignans (4.15 mg/100 g in extra-refined oil). There is also some evidence that olive oil contains flavonoids such as apigenin and luteolin (0.73 mg/100 g) [74; pp. 647-659].

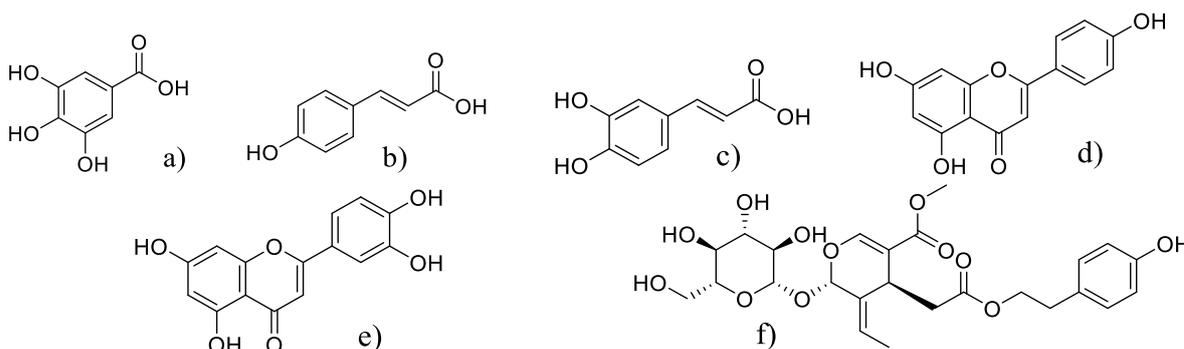


Figure 1.4. Some phenolic and flavonoid compounds found in olives: a) gallic acid; b) coumaric acid; c) caffeic acid; d) apigenin; e) luteolin; f) ligstroside;.

More than 70 compounds are considered to contribute to the characteristic aroma and taste of olive oil. These include aldehydes (particularly hexanal, nonanal, 1-hexanol or 2,4-decadienal), which are products of the degradation of unsaturated fatty acids. In addition, aliphatic and aromatic hydrocarbons, alcohols, ketones, esters, furans and thioterpene derivatives contribute significantly to the aroma and

taste of the oil [75; pp. 159-160].

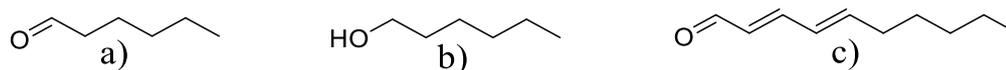


Figure 1.5. Some compounds that provide the aroma of olive oil: a) hexanal; b) 1-hexanol; c) 2,4-decadienal

Olive oil increases high-density lipoprotein concentrations and reduces low-density lipoprotein concentrations, and its compounds may provide primary and secondary protection against developing cardiovascular disease. In addition, it affects inflammatory biomarkers, such as tumor necrosis factor and interleukin-6, which are considered pro-inflammatory components of the human body [76; pp. 1-14].

Olive oil is low in free fatty acids, and regular consumption of it may reduce the risk of inflammatory diseases. It also helps reduce many other heart-related risk factors [77; pp. 663-670].

Oleic acid also protects the intestinal mucosa by reducing the production of hydrochloric acid, thereby preventing the formation of ulcers [78; pp. 17-41].

Olive oil contains some compounds, including vitamin E, which are present in small amounts and improve sensory and nutritional properties, as well as act as an antioxidant [79; pp. 19-28].

Environmental, genetic, and nutritional factors play a significant role in the development of gut microbiota. Extra virgin olive oil promotes gut health by supporting a rich biodiversity of gut microorganisms [80; pp. 1-6].

Researchers observed that mice fed olive oil had less neuropathology associated with Alzheimer's disease and a reduced risk of depression [81; pp. 580-591].

Researchers suggest that consuming olive oil may reduce the risk of developing breast cancer. In particular, it may prevent the onset of postmenopausal breast cancer [82; pp. 1-15].

Many studies have shown that minor components, which are abundant in extra-virgin olive oil, are more potent in exerting beneficial effects than the main

compounds. Olive oil exhibits properties that prevent many conditions, such as tumor growth inhibition, abnormal cell proliferation, and enhanced apoptosis [83; pp. 71-83].

There is considerable evidence that regular consumption of olive oil, due to its high content of monounsaturated fatty acids and polyphenols, is associated with a reduced risk of cardiometabolic diseases and type 2 diabetes [84; pp. 1-10].

Hydroxytyrosol is a major polyphenol compound present in olive oil, which exhibits anti-teratogenic and anti-inflammatory properties, as well as improving lipid status, activating inflammatory cells, and reducing oxidative stress [85; pp. 60-66].

The free radical scavenging effect of hydroxytyrosol was convincingly confirmed in studies conducted in alloxan – induced type 2 diabetic rats [86; pp. 8798-8804].

Oleuropein is another compound found in olive leaves and unripe fruits, and exhibits properties such as improved anti-inflammatory properties, antiproliferative properties by inducing apoptosis of cancer cells, and tumor inhibition [87; pp. 631-640].

The leaf is a major part of plant metabolism and can be considered as a potential source of bioactive compounds [88; pp. 260-286].

Many studies have been conducted focusing on the fact that olive leaves are rich in such valuable phenolic compounds [89; pp. 989-1009].

The phenolic compounds in olive leaves are numerous and diverse. They are divided into groups according to their molecular structure: simple phenols, acids, lignans, secoiridoids, flavonoids, including flavones (luteolin-7-glucoside, apigenin-7-glucoside, diosmetin-7-glucoside, luteolin and diosmetin), flavonols (rutin), flavan-3-ols (catechin), substituted phenols (tyrosol, hydroxytyrosol, vanillin, vanillic acid and caffeic acid) and oleuropein [90; pp. 632-638].

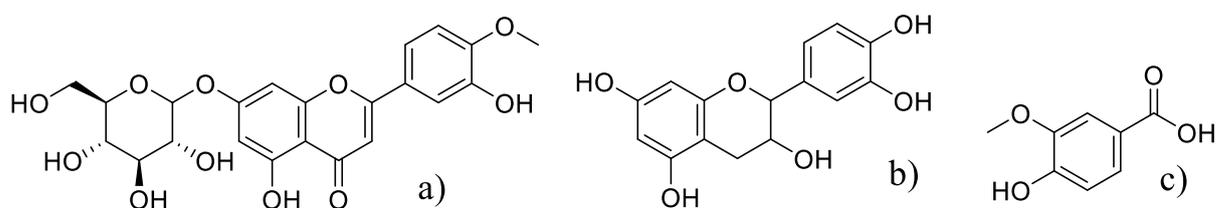


Figure 1.6. Structural formulas of flavonoids found in olives:  
a) diosmetin-7-glucoside; b) catechin; c) vanillic acid.

Several studies have demonstrated the anticancer properties of olive leaf extract in animal models. The leaf extract induces early apoptosis, which leads to necrosis in cancer cells [91; p. 488].

Synergism is observed when polyphenols present in olive leaf extract are combined with other antineoplastic agents. The anticancer effects of polyphenols present in olive oil, such as hydroxytyrosol and oleuropein, have been confirmed by numerous studies. These compounds inhibit the proliferation of cancer cells and induce cancer cell death, as seen in neuroblastoma, osteosarcoma, and breast cancer [92; 1955-1965].

From the above, it can be understood that it is not for nothing that olives have been widely used by mankind for various purposes since ancient times, especially in folk medicine due to their healing properties. Due to the many biologically active compounds they contain, obtaining a healing food supplement from them and using them in folk medicine remains an important task even today.

### § 1.6. Distribution, chemical composition and medicinal properties of flax plant in nature

Flax (*Linum usitatissimum L*) is an annual plant, reaching a height of 30-70 cm, and is considered one of the most useful crops. The stem grows erect, cylindrical, and branched. The leaves are sharp-pointed, lanceolate or linear, arranged alternately on the stem and branches. It blooms in April-May, and the fruits ripen in June-July [3; pp. 381-383].

Flax is one of the oldest crops, and its Latin name *Linum usitatissimum* means “Very useful.” Flax was first cultivated on a large scale in the United States

for the production of fiber for clothing. Various parts of flax, such as the seeds and the stem, have been used for various purposes, either directly or after processing. The stem yields high-quality fibers with high strength and durability [93; pp. 210-222].

Flax is available in the food market in various forms such as whole flaxseed, ground flaxseed, roasted flaxseed, and flaxseed oil. According to its chemical composition, flaxseed contains bioactive substances such as fats, protein, soluble polysaccharides, lignans, phenolic compounds, vitamins (A, C, F, and E), and minerals (P, Mg, K, Na, Fe, Cu, Mn, and Zn) [94; pp. 22-45].

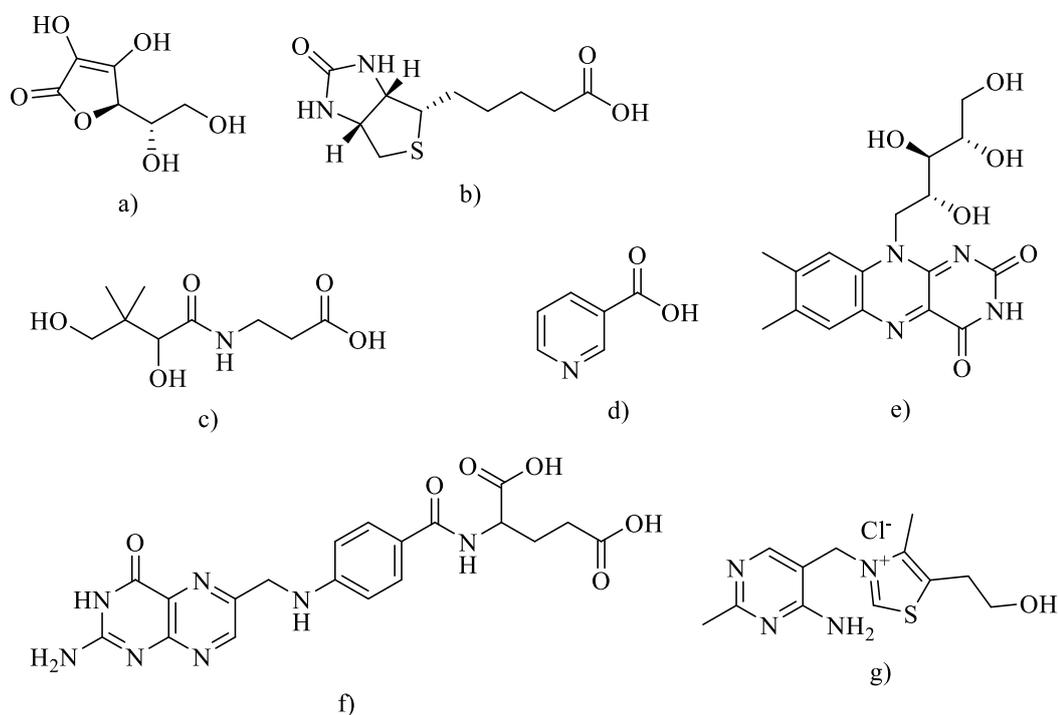


Figure 1.7. Some biologically active compounds found in flaxseed: a) ascorbic acid, b) biotin, c) pantothenic acid, d) nicotinic acid, e) riboflavin, f) folic acid, g) thiamine.

Flaxseed contains an average of 30-40% fat, 20-25% protein, 4-8% moisture, and 3-4% ash. Flaxseed is an important source of phenolic compounds, antioxidants such as flavonoids, lignins, high-quality protein, and soluble fiber, which are very beneficial phytochemically and affect cell growth and viability [95; pp. 129-140].

The composition of flaxseed oil typically consists of 9-10% saturated fatty acids (palmitic and stearic), about 20% monounsaturated fatty acids (mainly oleic acid), and more than 70% linoleic acid. Flaxseed oil is one of the richest sources of

polyunsaturated omega-3 fatty acids, and is a medicinal product with antioxidant and anti-inflammatory activities due to its unique chemical composition[96;].

In addition to its nutritional value, flaxseed is also recognized for its beneficial properties in the treatment of medical problems such as cardiovascular disease, hypertension, atherosclerosis, diabetes, cancer, arthritis, osteoporosis, autoimmune and neurological diseases due to its high concentration of  $\omega$ -3- $\alpha$ -linolenic acid, its richness in fiber, and its high content of lignans, which exhibit antioxidant and phytoestrogen properties [97; pp. 1633-1653].

Researchers have found that lignans in flaxseed inhibit the expression of the phosphoenolpyruvate carboxykinase gene, which encodes a key enzyme responsible for glucose synthesis in the liver [98; pp. 107-109].

Another study found that adding 10 g of flaxseed powder daily to the diet of patients with type 2 diabetes for 1 month reduced blood glucose levels by 19.7% and glycosylated hemoglobin levels by 15.6% [99; pp. 257-265].

Flaxseed oil is well known for its high content of  $\alpha$ -linolenic acid, which is a high source of  $\omega$ -3, proteins, and antioxidants, which may protect against inflammation and accelerate wound healing by inhibiting inflammation [100; pp. 32–40].

From the above information, it is clear that flaxseed, in various forms such as ground seeds and oil, is a very beneficial product for health due to its rich chemical composition. The study of its use in folk medicine in the treatment of diabetes and inflammatory diseases has not lost its practical importance even today.

### **§ 1.7. Diabetes, its types and causes, and the use of saffron in its treatment**

Diabetes mellitus is a disease characterized by a persistent, chronic increase in blood sugar levels. In diabetes mellitus, blood sugar levels increase sharply and are excreted in the urine, leading to thirst, weight loss, weakness, itching, and other symptoms [1; pp. 339-340].

There are several types of this disease. However, the most common types of diabetes in patients are type 1 and type 2. Type 1 occurs mainly in infants and

adolescents. It occurs as a result of an absolute deficiency of the hormone insulin produced by the pancreas. The occurrence of type 1 can be caused by several viral diseases experienced in childhood. Type 2 diabetes occurs mainly in adults. It occurs as a result of a relative deficiency of the hormone insulin produced by the pancreas. The main goal of treatment in both types of diabetes is to bring blood sugar levels as close as possible to those in healthy people, that is, to achieve a state of compensation [2; p. 254].

In medicine, the main active substrate for the treatment of diabetes mellitus is synthetic drugs such as biguanides, sulfonylureas, thiazolidinediones, miglitol, acarbose, glimepiride. Although the above drugs are effective in reducing blood sugar levels, most of these drugs have a number of serious adverse effects, such as increased liver enzymes, weight gain, edema, mild anemia. In addition, the main disadvantage of these drugs is that they must be given for life and cause serious side effects. Thus, it is still difficult to manage diabetes without side effects, so it is important to search for alternative drugs such as medicines from natural products [101; pp. 2658-2637].

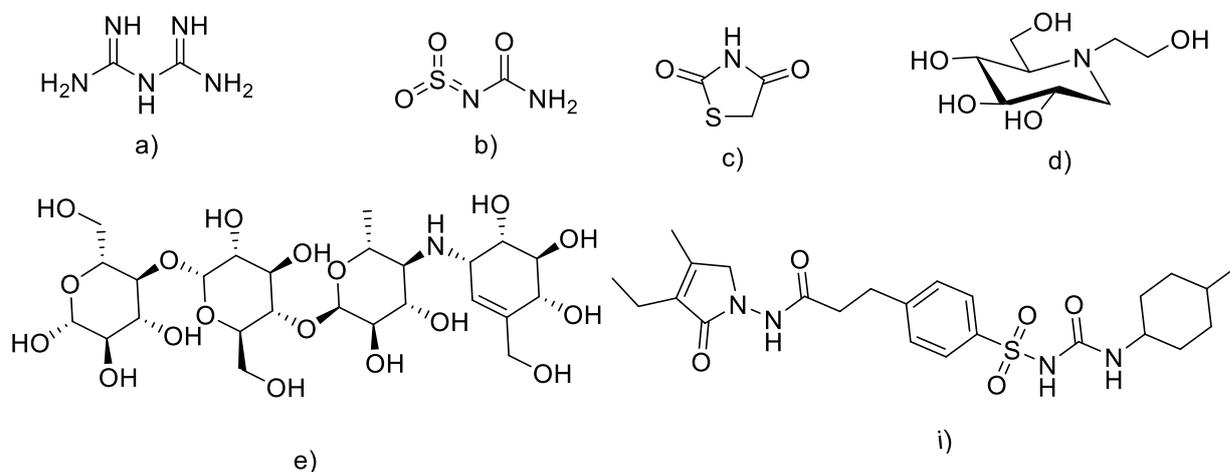


Figure 1.8. Structural formulas of some drugs used in diabetes: a) biguanide; b) sulfonylurea; c) thiazolidinedione; d) miglitol; e) acarbose; i) glimepiride.

In folk medicine, several food supplements are recommended for the treatment of diabetes: “Majmui Rahmaniyy”, “Askalis”, “Oltin vodiyy”, “Alkaman”, “Shifoi bashim”, “Astosh”, “Tog’ guli”. Also, products such as pumpkin, mung bean, barley, peas, grape skins, fig leaves, plum leaves, corn cobs and bitter melon,

as well as infusions prepared from them, are widely used due to their positive benefits [3; pp. 1010-1011].

A number of biomedical research studies have shown that saffron and its components may be beneficial in neurodegenerative diseases and related memory impairment, ischemic retinopathy, coronary artery disease, blood pressure, acute or chronic inflammatory diseases, depression, seizures, and parkinsonism [30; pp. 426-432].

The hypoglycemic effect of saffron is mediated by mechanisms such as stimulation of glucose uptake by peripheral tissues and increased insulin production by  $\beta$ -cells of the islets of Langerhans, as well as inhibition of intestinal glucose absorption, insulinase activity in the liver and kidneys, endogenous glucose production, and renal glucose reabsorption or reabsorption [102; pp. 541-549].

Researchers have shown that saffron consumption reduces glycosylated hemoglobin levels and also increases insulin sensitivity by activating GLUT4 (glucose transporter 4) [103;].

Saffron also helps to prevent complications caused by diabetes. The mechanism by which glucose causes neurotoxicity is not yet fully understood. Researchers have found that saffron may reduce the effects of diabetic neuropathy by reducing phospholipids [104; pp. 185-191].

Scientific studies aimed at determining the medicinal properties of saffron have shown that it has significant antidiabetic activity. This can be explained by the presence of biologically active compounds belonging to the carotenoid class, such as crocin, crocetin, safranal and  $\beta$ -carotene, in saffron [105; pp. 39-43, 106; pp. 1042-1047].

Carotenoids, the main source of yellow, orange, and red plant pigments, are widely distributed in nature. Carotenoids are widespread phytochemicals that play important roles in various metabolic processes. They are considered essential compounds for life, mainly due to their diverse metabolic functions. Carotenoids are found in all living organisms, from bacteria and algae to higher plants, in

photosynthetic and non-photosynthetic tissues, as well as in most commonly consumed vegetables and fruits [107; p. 181].

Carotenoids are divided into two groups: carotenes and xanthophylls. Carotenoids, such as  $\alpha$ -carotene,  $\beta$ -carotene,  $\gamma$ -carotene, and lycopene, are hydrocarbons. There are about 50 types of carotenes in nature. On the other hand, xanthophylls, such as  $\beta$ -cryptoxanthin, lutein, zeaxanthin, astaxanthin, fucoxanthin, and peridinin, are carotenoids containing oxygen atoms in these groups, such as hydroxy, carbonyl, aldehyde, carboxylic, epoxide, and furanoxide [108; pp. 191-195].

In recent decades, carotenoids (lycopene,  $\beta$ -carotene, lutein, zeaxanthin, and  $\beta$ -cryptoxanthin) have attracted great interest in the fields of human nutrition, as they are biological antioxidants that contribute to the protection of the body against atomic oxygen species and play a protective role in diseases such as diabetes and cardiovascular diseases [109; pp. 1668-1677].

It is clear that the treatment of diabetes focuses on reducing blood sugar levels by increasing insulin secretion and increasing the human body's sensitivity to it. Compounds such as crocetin, crocin, zeaxanthin, and carotenes in saffron florets have hypoglycemic properties. Therefore, determining the amount of these compounds in saffron and using saffron in the treatment of diabetes may be effective in the future.

### **§ 1.8. Prospects for the treatment of Parkinson's disease (tremor paralysis) with saffron in folk medicine**

Parkinson's disease is a chronic disease of the central nervous system. In a person with this disease, the muscles become tense, the face becomes immobile, and in simple terms, the patient's movements are limited. Tremors are most often observed in the hands, feet, jaw, tongue, and eyelids. This disease is more common among men [1; pp. 749-750].

Parkinson's disease is a neurodegenerative disease. Currently, there are many tools, including surgery, to treat the early and late complications of

Parkinson's disease . Future developments in Parkinson's disease will likely focus on the concept of drugs that provide neuroprotection. [110; p. 125].

According to reports from the World Health Organization, the incidence of Parkinson's disease has doubled in the last 25 years, and by 2019, the disease had caused disability in 5.8 million people and the death of 329,000 patients [111; p. 1].

Medicines such as Apomorphine, Ropinirole, Pramipexole, Levodopa, Entacapone, Rasagiline are used. However, these drugs have side effects such as drowsiness, nausea, vomiting, dizziness, swelling of the legs, sweating, diarrhea, hallucinations, dry mouth, and abdominal pain [112; p. 801].

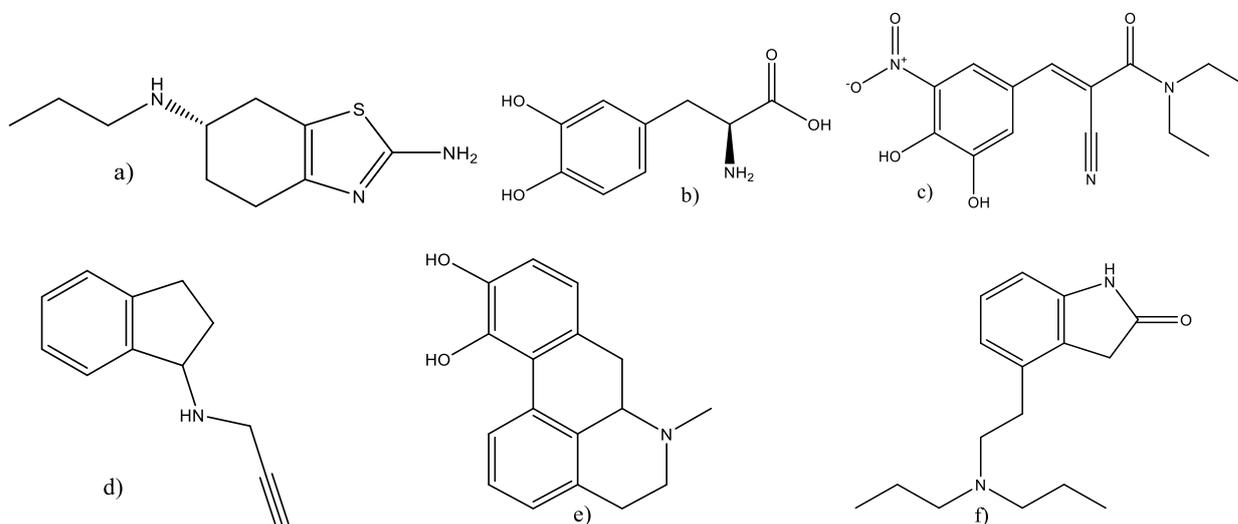


Figure 1.9. Chemical formulas of some synthetic drugs used in medicine to treat Parkinson's disease: a) pramipexole; b) levodopa; c) entacapone; d) rasagiline; e) apomorphine; f) ropinirole;

In addition to modern medical treatments, natural remedies can also be used. For example, regular consumption of natural, biologically active food supplements such as Shifoi Basi, Nishifo, Asdavo, Askalsiy, Antivir 101 is effective in treating tremors and paralytic diseases [1; p. 750-751].

Saffron has been used in folk medicine for centuries to treat and prevent a number of diseases, including headaches, bronchitis, kidney stones, nasal diseases , impotence , liver cirrhosis, sexual weakness, bleeding gums, seizures, and heart diseases. It is a plant that has not lost its importance and value in modern medicine. [ 3; p. 379].

There is scientific evidence in the literature that saffron affects several important mechanisms of Parkinson's disease pathogenesis, has a therapeutic effect on the aggregation of alpha-synuclein, a neuroprotein that regulates monoamine homeostasis, eliminates inflammatory markers, and reduces apoptosis of dopaminergic neurons [113;].

Saffron flower buds have been found to have antioxidant activity, making saffron a promising natural product in this regard. Saffron flower buds contain some flavonoids, which contribute to the antioxidant activity of saffron [114; p. 6253].

Flavonoids are found in many plant species . They are a major part of the daily diet, including vegetables, fruits, nuts, seeds, stems, flowers, tea, and wine [115; p. 240].

In addition to the use of gallic acid and its ester derivatives in the food industry as flavoring agents and preservatives, there is diverse scientific evidence regarding the biological and pharmacological activities of these phytochemicals, such as antioxidant, antimicrobial, anti-inflammatory, anticancer, cardioprotective, gastroprotective, and neuroprotective effects [116; p. 226].

Rutin is a flavonol, abundant in plants such as buckwheat, tea, and apples, and is an important component of food products. Chemically, it is a glycoside and has demonstrated a number of pharmacological activities, including antioxidant, cytoprotective, vasoprotective, anticarcinogenic, neuroprotective, and cardioprotective activities [117; p. 151].

Studies have shown that quercetin has several beneficial biological activities, such as antioxidant, anti-inflammatory, anticancer, and antiviral properties [118; p. 147].

Literature review shows that apigenin has several important pharmacological activities, including those against diabetes, cancer, and insomnia [119;].

Several studies support the role of kaempferol in the prevention and treatment of other diseases, such as neurodegenerative diseases, infectious diseases, diabetes, osteoporosis, allergies, inflammation, and pain [120; p. 326].

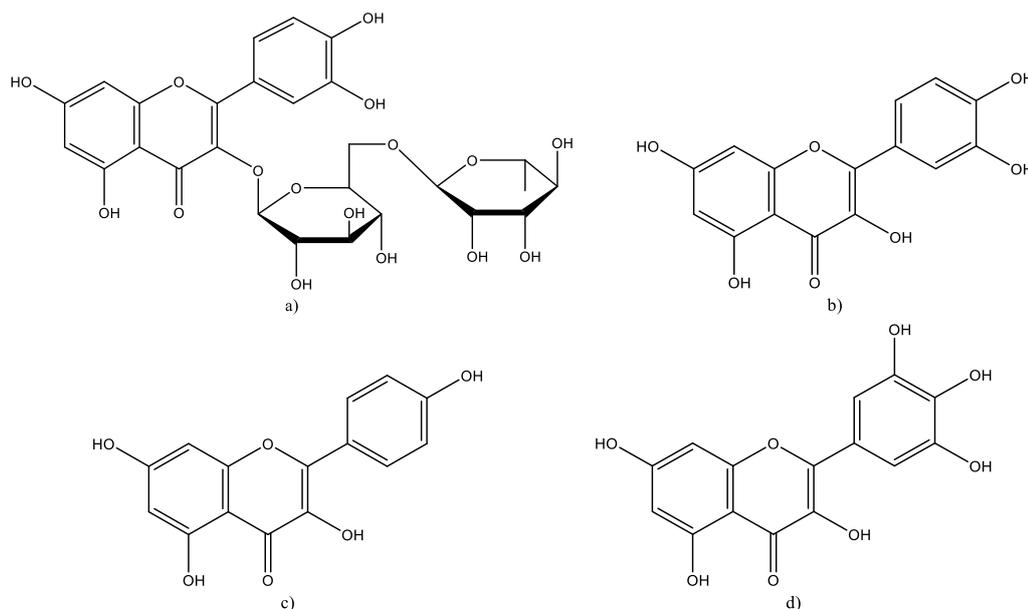


Figure 1.10. Structural formulas of some representatives of flavonoids: a) rutin; b) quercetin; c) kaempferol; d) myricetin.

Parkinson's disease is a disease associated with a disruption in the functioning of the central nervous system. Saffron marigolds contain a number of compounds with neuroprotective properties. This suggests that marigolds may be a good option for preventing, treating, and reducing the harmful effects of Parkinson's disease.

### § 1.9. The use of olive oil in folk medicine to treat inflammation, kidney stones, and cardiovascular diseases

Inflammation is a complex reaction of the human body that protects against the effects of harmful factors that cause disease. Although inflammation is a protective adaptive reaction, under certain conditions it can lead to damage to tissues necessary for the body [1; p. 853].

infection, tissue injury, or myocardial infarction, can cause inflammation by damaging tissues. Bacteria, viruses, and other microorganisms cause infectious inflammation, while burns, frostbite, trauma, ionizing radiation, as well as glucose, toxins, alcohol, and chemical irritants can cause noninfectious inflammation [121; p. 7204].

Inflammation is characterized by five main signs based on visual observations: redness, swelling, warmth, pain, and loss of joint function. The

sensation of warmth results from increased blood flow through dilated vessels to cooler areas, which in turn causes increased redness due to the additional number of red blood cells passing through the area. Loss of joint function refers to the loss of normal joint mobility due to swelling and pain or the replacement of functional cells with scar tissue [122].

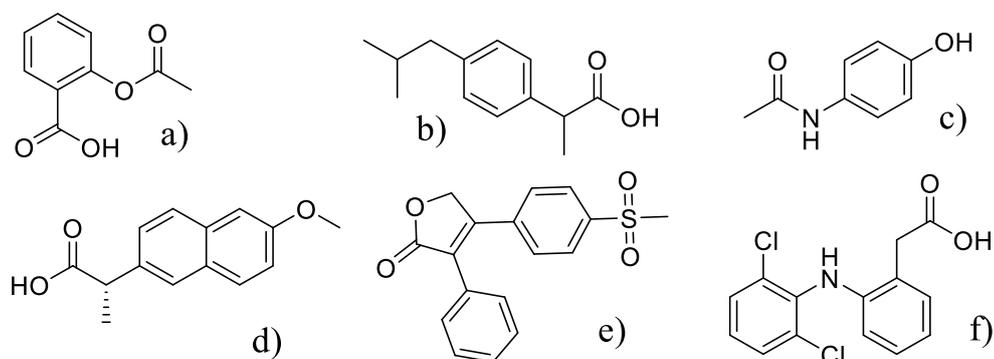


Figure 1.11. Structural formulas of some synthetic agents used in inflammation: a) aspirin; b) ibuprofen; c) acetaminophen; d) naproxen; e) rofecoxib; f) diclofenac.

Synthetic anti-inflammatory drugs are generally toxic to the body, especially to the stomach and kidneys. Studies in rat models have shown that aspirin can damage the gastrointestinal system. High doses of ibuprofen have been shown to cause perforation of the small intestine, even in short courses. The combination of ibuprofen and acetaminophen, even at therapeutic doses, has been shown to cause kidney and liver problems. Another anti-inflammatory drug, naproxen, has been shown to cause antral ulcers and increased lipid peroxide levels. Another drug, rofecoxib, has been associated with an increased risk of kidney and arrhythmias. Diclofenac has been shown to increase the risk of heart attack and stroke by 50% [123; p. 253].

Therefore, folk medicine recommends natural products that are free from side effects as anti-inflammatory agents. In particular, the use of food supplements ASKALSIY, ASSHIFO, OLTIN VADIY, NISHIFO has been proven to be effective in treating inflammation. Also, infusions made from plants such as pine buds, clover, white acacia flowers, etc. can be used to treat inflammation [2].

In folk medicine, the role of olive oil in the treatment of ringworm is unparalleled due to its rich chemical composition.

The results of studies conducted by Iranian scientists have shown that olive oil can be effective in treating kidney inflammation by improving kidney function and tubular necrosis [116; pp. 1327-1333].

Malaysian researchers point out that there are several studies that prove that olive oil has beneficial effects in respiratory diseases by attenuating cytokines and oxidative stress due to its antioxidant and anti-inflammatory properties [125].

Biophenols in olive oil exert direct antioxidant effects in the intestine and modulate intestinal epithelial homeostasis by exerting beneficial effects on the inflammatory process and the intestines [126; p. 4085].

Analysis of the results of various *in vivo* and *in vitro* experiments conducted by many researchers has shown that olive oil can reverse or limit the development of prostatic inflammation due to the free radical-scavenging phenolic and polyphenolic compounds contained in it [127].

The phenolic composition of extra-refined olive oil is more complex, containing alcohol derivatives of phenol, hydroxytyrosol, tyrosol and their esters secoiridoids, oleacein and oleocanthal. [128; pp. 81–115].

Oleacein is the main antioxidant polyphenol compound commonly found in QTZM, and also has partial anti-inflammatory activity [129; pp. 401–415].

This compound is also present in olive leaves and can be obtained in high yields by simple extraction methods, suggesting that oleacein may be a good raw material for the development of new anti-inflammatory drugs [130; pp. 4214–4219].

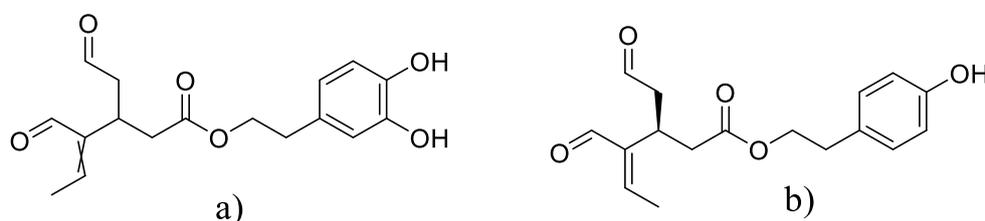


Figure 1.12. Structural formulas of a) oleacein and b) oleocanthal.

Renal calculi are the most common urinary tract disease, known to mankind since 4000 BC. Urinary calculi affect 12% of the world's population during their

lifetime. They are associated with a high risk of chronic kidney disease, end-stage renal disease, cardiovascular disease, diabetes, and hypertension [131].

Kidney stones are small crystals of various chemical compositions. The crystals grow and enlarge as a result of a constant lack of fluid intake. Typically, stones range from 4 mm to 4-5 cm in size [1; p. 94].

The composition of kidney stones depends on the chemical composition of urine and they vary in size, shape, and chemical composition. Stones are often divided into five groups based on their mineral composition and pathogenesis: calcium stones, struvite or magnesium ammonium phosphate stones, uric acid stones, cystine stones, and drug-induced stones [131].

Treatment of the disease is carried out by one of the following methods, based on the results of a urological examination, with the use of drugs aimed at the independent passage of the stone, drug therapy aimed at dissolving the stone, distension shock wave lithotripsy, endoscopic contact lithotripsy, percutaneous nephrolithotripsy, endoscopic surgery, or open surgical interventions [1; p. 94].

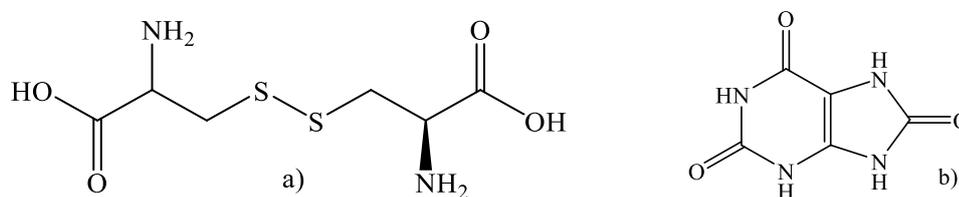


Figure 1.13. Structural formulas of cystine (a) and uric acid (b)

In the treatment and prevention of relapse of the disease, some synthetic agents are used in medicine, such as hydrochlorothiazide, triamterene, amiloride, etc., which belong to the thiazide class. While they are useful, they are observed to cause several adverse side effects, including dizziness, weakness, fatigue, thirst, nausea, vomiting, diarrhea or constipation, rashes, skin reactions, etc. The most dangerous effect of potassium drugs is hyperkalemia, especially in patients with renal failure. This can be life-threatening, especially in combination with potassium-sparing diuretic therapy [132; pp. 1865–1877].

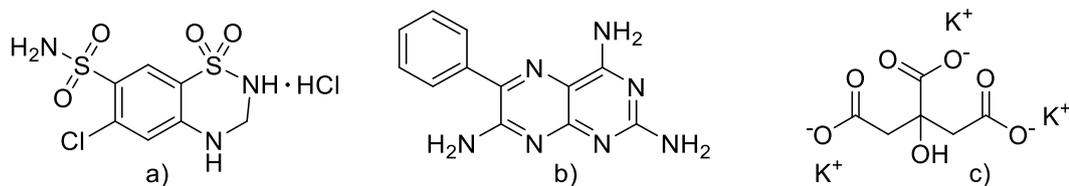


Figure 1.14. Structural formulas of some drugs used in nephrolithiasis: a) hydrochlorothiazide; b) triamterene; c) potassium citrate

In folk medicine, various methods are used to treat kidney stones. For example, decoctions of biologically active food additives such as Astosh, Airitosh, Shifo, Altin vodi, Shifoi sabs, Antivir and regular consumption can achieve high results. Also, ointments and tinctures made from natural products such as radish, turnip, corn, sunflower, peach kernel, oats, pumpkin, melon, melon seeds, garimdori (pepper), honey are considered good means for treating the disease in folk medicine [1; p. 94-95] dried apple peels or by drinking apple juice several times a day [3.1017-b.]

Also, in folk medicine, the use of olive oil in the treatment of kidney stones is also effective. It is necessary to drink two tablespoons of olive oil every day. If you drink two tablespoons of olive oil warmed half an hour or an hour before meals, it is useful in dissolving kidney stones and preventing the disease [133. 26-b].

Oxidative stress is a relatively new concept that has been widely used in medical science in the last three decades. It is actively involved in the physiology of such common diseases as diabetes, hypertension, atherosclerosis, acute renal failure, Alzheimer's and Parkinson's diseases [134; p. 3380].

The development of kidney disease can also be caused by oxidative stress, which occurs due to an imbalance in the production of free radicals and antioxidants in the body. Many studies have shown that olive oil, fruit, leaves and their components such as oleuropein, hydroxytyrosol, oleic acid have antioxidant and anti-inflammatory activities [135;].

Cardiovascular diseases are the most common diseases, and they can sometimes be very serious. Such diseases are mainly accompanied by pain, shortness of breath, rapid and uneven heartbeat, swelling, coughing up blood,

dizziness, and pain. The pain is most often felt in the heart area, under the right and left ribs, and in the legs [1; p. 839].

Cardiovascular disease has a multifactorial etiology and is associated with various risk factors for its development, including hypercholesterolemia, hypertension, smoking, diabetes, poor diet, stress, and physical inactivity [136; p. 91].

Atherosclerosis is a vascular disease characterized by the narrowing and dysfunction of the major (large) arteries. Poor nutrition, inactivity, and stressful situations contribute to the development of atherosclerosis [1; pp. 18-19].

atherosclerosis suggest that the disease may be associated with free radical reactions involving lipids produced during dietary intake in the arterial wall and in the blood serum to produce peroxides and other substances. These compounds cause endothelial cell damage and cause changes in the arterial wall [137; p. 119].

Another cardiovascular disease is myocardial infarction, which occurs when blood flow to the heart muscle through the coronary arteries is reduced or completely absent [1; p. 450].

Hypertension is another cardiovascular disease. This disease is a complex primary condition characterized by cardiovascular pathology, unstable and progressive increase in arterial pressure, and subsequent morphological changes in the body [1; p. 127].

Synthetic drugs such as Pentoxifylline, Aspirin, Idrinol, Lorista are used in cardiovascular diseases. Pentoxifylline can cause nausea, vomiting, itching, and dizziness, Aspirin can cause stomach upset, ulcers, stomach bleeding, and worsening of asthma, Idrinol can rarely cause tachycardia, decreased or increased blood pressure, itching, rash, and hyperemia of the skin, Lorista can often cause dizziness, headache, and insomnia [138; p.513, 139; 246., 140; p.108., 141; p.15.].

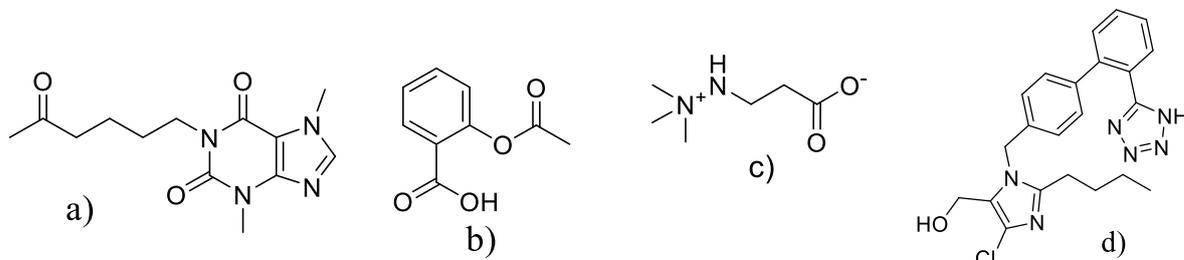


Figure 1.15. a) pentoxifylline; b) acetylsalicylic acid; c) idrinol (mildronate); d) lorista.

In folk medicine, a number of natural products are used to treat cardiovascular diseases, including the biologically active food supplements «Majmui Rahmani», «Alkoman», «Astosh», «Shifoibosim», «Shifo» [1; p. 839].

Z aytun also has a beneficial effect on the above diseases due to the presence of oleic acid, linoleic acid, oleuropein, vitamin E, and various flavonoids [142;].

The damaging properties of free radicals contribute to the etiology of many chronic health problems, including cardiovascular and inflammatory diseases, cataracts, and cancer. Antioxidants prevent tissue damage caused by free radicals by preventing their formation, scavenging them, or promoting their degradation [136; p. 124].

A free radical can be defined as a molecular particle that has an unpaired electron in an atomic orbital and can exist independently. Free radicals attack important macromolecules, causing cellular damage and homeostatic disturbances [143; p. 218].

One of the biological mechanisms to counteract oxidative stress is the production of antioxidants.  $\alpha$  - tocopherol is a potent peroxy radical scavenger and protects cell membranes from lipid peroxidation [144; p. 254].

Flavonoids are polyphenolic compounds found in many plants. The beneficial effects of flavonoids on human health are mainly due to their potent antioxidant activity. They have been reported to prevent or delay a number of chronic and degenerative diseases, including cancer, cardiovascular disease, arthritis, aging, cataracts, memory loss, stroke, Alzheimer's disease, inflammation, and infection [137; p. 94].

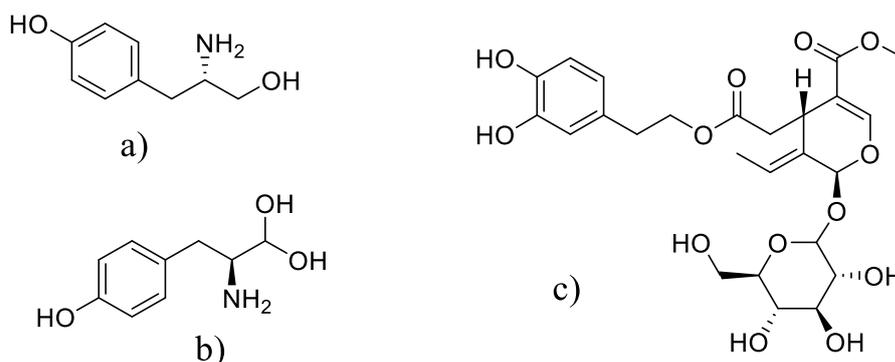


Figure 1.16. a) tyrosol; b) hydroxytyrosol; c) oleuropein.

Olive oil is considered very healing due to its content of triglycerides of unsaturated acids, oil-soluble vitamins, and a number of biologically active compounds contained in small quantities. Creating therapeutic food additives from it for the treatment of various forms of inflammation is one of the urgent tasks of folk medicine today.

### Conclusions on Chapter I

1. Traditional medicine has been improved and tested over the centuries, but it has not lost its relevance.

2. Although the use of synthetic agents in the treatment of diabetes and inflammatory diseases is effective, their negative side effects necessitate the search for alternative, harmless natural agents.

3. Olive (*Olea europaea*) and saffron (*Crocus sativus L.*) plants, new food additives with anti-inflammatory and blood sugar-lowering properties have been created, and TIF TN code numbers have not been developed as a commodity.

4. Saffron (*Crocus* The chemical composition and medicinal properties of the plant (*Sativa sativus L.*) were studied. It became clear that it is necessary to develop food additives that can be used in diabetes.

5. The distribution, chemical composition, and medicinal properties of the olive (*Olea europaea*) plant in nature were analyzed, and it became clear that there is a need to develop food additives with anti-inflammatory properties.

6. Flax, in its various forms such as roasted, ground, whole seeds and oil, is a very beneficial product for health due to its fatty acids, protein, vitamins, various

organic biologically active compounds and minerals. The study of its potential use in folk medicine for the treatment of diabetes and inflammatory diseases remains an urgent issue that has not lost its practical importance today.

7. Diabetes mellitus, its types and causes, and the harmful effects of synthetic drugs used to treat it, therefore, it is necessary to explore the possibilities of using saffron in diabetes.

8. A number of compounds in it have been found to have the ability to protect brain cells due to their antioxidant properties.

9. It has become clear that a number of synthetic drugs used for various inflammatory diseases have side effects, and that it is necessary to develop a natural healing food supplement based on olive oil to combat various inflammatory conditions in the body.

## CHAPTER II. RESULTS OF EXPERIMENTS CONDUCTED AT RESEARCH OBJECTS AND THEIR DISCUSSION

### §2.1. Elemental analysis of saffron stigmas

The content of macro and microelements in saffron crocuses grown in the Surkhandarya region of the Republic of Uzbekistan was determined using the optical emission spectrometry method. The reason for choosing this method is The use of inductively coupled plasma-optical emission spectrometry (ICP-OES) for inorganic elemental analysis is very popular in the field of chemical analysis. The advantages of using this method are wide elemental coverage, very low detection limits, fast analysis times (sometimes all elements simultaneously), wide analytical working range, simple spectra of constituent elements, and high matrix tolerance [145; pp. 45-54].

During the analysis, 29 elements were examined (Table 2.1.), and 15 of them were found to be present in varying amounts in saffron crocuses. The following table presents the data obtained as a result of the analysis:

Table 2.1.

Elemental analysis results of saffron crocuses

T/r	Item name	Character	Quantity (mg/100 g)	T/r	Item name	Character	Quantity (mg/100 g)
1	Phosphorus	P	432.2±0.72	9	Aluminum	Hand	21.23±0.22
2	Potassium	K	375.4±0.54	10	Sodium	No	20.15±0.28
3	Magnesium	Mg	160.3±0.34	11	Manganese	Mn	2.38±0.12
4	Calcium	Ca	111.5±0.28	12	Strontium	Sr.	1.225±0.24
5	Zinc	Zn	74.325±0.46	13	Copper	Cu	1.025±0.18
6	Sulfur	S	35.87±0.38	14	Yes	B	0.675±0.09
7	Tellurium	The	28.05±0.48	15	Lithium	Lee	0.139±0.06
8	Iron	Fe	26.04±0.36				

Analysis based on structured in the table k o' is shown to the information ko'ra this to say maybe we from us checked saffron flower beaks in the composition the most many occurring element phosphorus that is known his body, his quantitative value per 100 grams 432.2 mg in the sample what organization does. In the next places potassium 375.4 mg, magnesium 160.3 mg and calcium

111.5 mg value with saffron beak in the content the most many in quantity there is was elements row organization reached.

Saffron stilts in the composition per 100 g this is it contains 1-100 mg in quantity occurring elements row such as zinc (74.3 mg), sulfur (35.87 mg), tellurium (28.05 mg), iron (26.04 mg), aluminum (21.23 mg), sodium (20.15), manganese (2.38 mg), strontium (1.225 mg), copper (1.025) elements organization reached.

Lithium (0.139 mg) and boron (0.675 mg) 1 mg /100 g from the value less occurring elements that is known was, antimony, molybdenum, selenium, tin, barium, chromium, arsenic, lead, cadmium, vanadium, silver, mercury, cobalt and nickel elements this is it in the composition not found.

Many in research sugary in diabetes micronutrients in the blood glucose level to reduce effect observed they are carbohydrate in exchange participation provider enzyme systems for cofactors as and insulin sensitivity to increase service does [146; pp. 21-27].

Spanish scientists by in children take visited in research blood serum in the content zinc ions amount enough at least insulin activity reduction, zinc ions amount enough when it happens and insulin activity level increase This study suggests that zinc may improve health by increasing insulin activity [147; pp. 398-404].

Several studies have shown that magnesium is important in diabetes and that it improves insulin secretion and glucose metabolism. Researchers suggest that magnesium-containing products may improve insulin sensitivity and blood glucose levels in diabetic patients with magnesium deficiency [148; pp. 39-52].

Some studies have shown that copper deficiency is associated with an increased risk of complications in diabetic patients. This important trace element is involved in the production of antioxidants that reduce the harmful effects of free radicals [149; pp. 1735-1746].

As a result of analyzing the content of macro and microelements in saffron crocuses grown in our country using optical emission spectrometry, 15 out of 29

elements tested were present in varying amounts, 71.283 mg/100g more than in saffron crocuses grown in Iran, and sodium was 0.27 mg/100g more than in saffron crocuses grown in Iran. It is also important to note that elements such as manganese (2.38 mg/100g) and copper (1.025 mg/100g), which are important for the production of insulin in the body, increasing its activity, and reducing the complications of diabetes, were also detected.

## 2.2 -§. Determination of $\beta$ -carotene content in saffron stigmas

A spectrophotometric method was used to determine the amount of  $\beta$ -carotene in saffron crocuses adapted to the Surkhandarya region of the Republic of Uzbekistan.

Analysis of literature data shows that carotenoids are soluble in ethyl alcohol, acetone, hexane, chloroform, and other organic solvents [150; pp. 112-119].

The main absorption maximum in hexane is at a wavelength of 450 nm for  $\beta$ -carotene. The optimal conditions for quantitative determination of  $\beta$ -carotene are as follows: extractor – hexane; raw material – extractant ratio – 1:5; extraction time – within 90 minutes; raw material grinding degree 0.5 mm [151; 139-144-p.].

The  $\beta$ -carotene content of saffron florets was determined based on the above information.

Based on the results presented in Table 2.2., it can be concluded that the optimal conditions for determining the amount of  $\beta$ -carotene in saffron crocuses are hexane as the solvent, sample and solvent ratio of 1:5, sample grinding degree of 1 mm, and extraction time of 90 minutes.

Table 2.2.

Results of quantitative analysis of  $\beta$ -carotene in saffron crocuses

Solvent	Sample and solvent ratio	Grinding rate (mm)	Extraction time (minutes)	$\beta$ -carotene content ( $\mu\text{g/g}$ )
The effect of the solvent				
Hexane	1:5	1	90	416 $\pm$ 7.6
Acetone	1:5	1	90	72.1 $\pm$ 3.6
Ethyl alcohol (96%)	1:5	1	90	29.9 $\pm$ 1.8

Ethyl acetate	1:5	1	90	216.5±6.9
Chloroform	1:5	1	90	213±7.2
Effect of sample and solvent ratio				
Hexane	1:1	1	90	126.7±3.4
Hexane	1:10	1	90	401.5±6.8
Hexane	1:15	1	90	329.5±5.4
The effect of grinding level				
Hexane	1:5	0.5	90	402.8±5.2
Hexane	1:5	1.5	90	390.6±4.8
Hexane	1:5	2	90	365±2.6
Hexane	1:5	2.5	90	342.5±6.2
Effect of extraction time				
Hexane	1:5	1	30	269.2±4.4
Hexane	1:5	1	60	330.4±5.2
Hexane	1:5	1	90	416±7.6
Hexane	1:5	1	120	391.5±5.1

Literature analysis this It shows that different in countries cultivated saffron examples in the content one how much carotenoids, in particular  $\beta$  - carotene is available (Table 2.3.) [152; pp. 34-40].

Table 2.3.

The content of some carotenoids detected in different ecoforms of saffron crocus

Regions	Crocin mcg/g	Crocetin mcg/g	$\beta$ -carotene mcg/g	Zeaxanthin mcg/g
India	311.6	Not found	Not found	Not found
Turkey	8201.7	186.6	512.9	252.0
Iran	11141.6	1054.7	343.4	61.2

Based on the above result, we will be able to compare the amount of  $\beta$ -carotene in saffron stigmas grown in our country with the amount of  $\beta$ -carotene in other regions.

The following to the picture ko'ra local (Surkhandarya) saffron in the beaks  $\beta$  – carotene amount Turkey to the saffron relatively less than Iran's and more (India - Kashmir) saffron in the composition not found) known will be [153; pp. 27-31].

$\beta$  – carotene is a carotenoid that is abundant in the human diet and is found in all tissues of the human body, including the blood. Due to its high biological activity, it is also widely used in medicine [154; pp. 727-743].

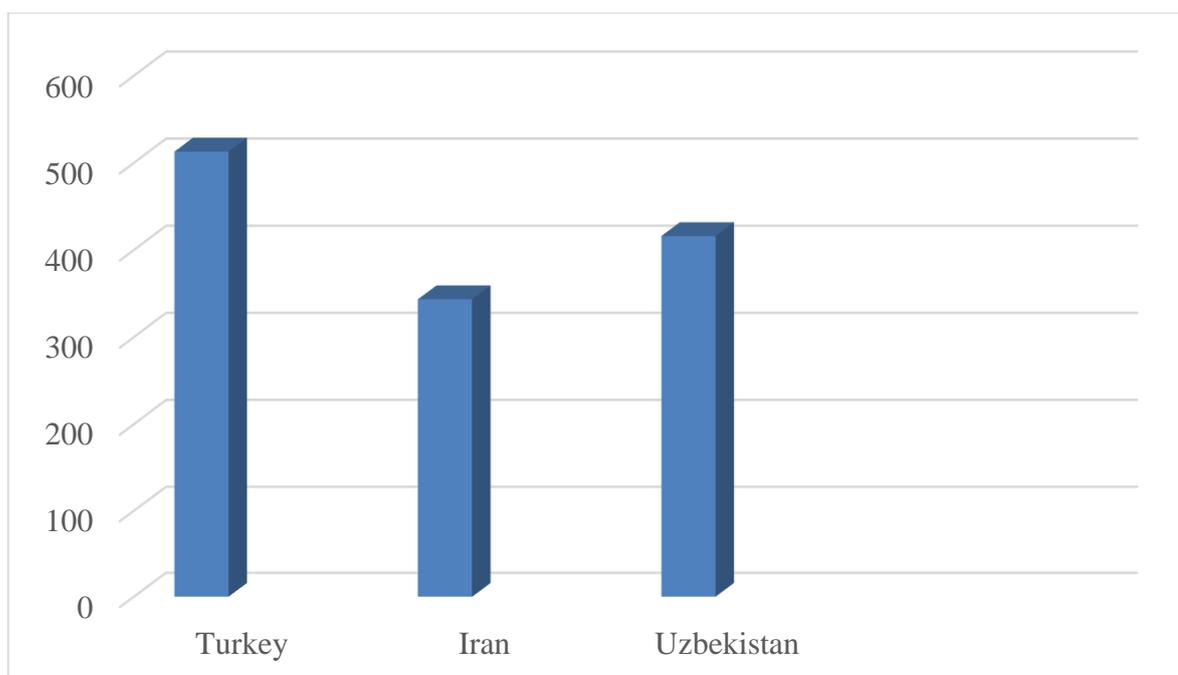


Figure 2.1. Comparative analysis of the content of  $\beta$ -carotene in different ecoforms of saffron crocus

Among the many functions of  $\beta$ -carotene in the human body, the most important is its participation in the provision of provitamin A, which affects the development, proper growth and vision of the embryo. In addition, it exhibits anticancer and antioxidant properties [155; pp. 511-517].

Given the excessive increase in CFA in diabetes, a number of scientists have found that adding products containing  $\beta$ -carotene to the diet of patients can adequately counteract the harmful effects of their CFA [156; pp. 157-161].

$\beta$ -carotene in plant products considered beneficial and recommended for diabetes varies, from 10  $\mu\text{g/g}$  in groundnut to 55.8  $\mu\text{g/g}$  in stevia [157; 158].

According to the results of spectrophotometric analysis of the  $\beta$ -carotene content of saffron crocuses grown in our country it was found that the  $\beta$ -carotene content of these saffron crocuses is 1.21 times higher than that of Iranian saffron. It can also be understood that it is 41.6 times higher than that of ground pears, which are known to be beneficial for diabetes, and about 7.5 times higher than that of stevia leaves.

### §2.3. Determination of the content of some flavonoids in saffron stigmas

The superiority of UV-vis spectroscopy as a primary analytical method is not accidental. Its most obvious advantage is its applicability to a wide range of sample types, from small organic molecules and ions to large biomolecules and polymers. UV-vis spectroscopy is becoming a standard platform technology for rapid bioanalytical testing, macro- and micronutrient analysis in food products, and forensic and environmental sample studies. The high accuracy and reliability of UV-vis spectroscopy, which detects UV radiation, have also made it an indispensable tool in the field of quality control [159; pp. 472-479].

the above information, we aimed to analyze the amounts of gallic acid, rutin, quercetin, apigenin, and kaempferol in saffron crocuses and performed the analysis using high-performance liquid chromatography.

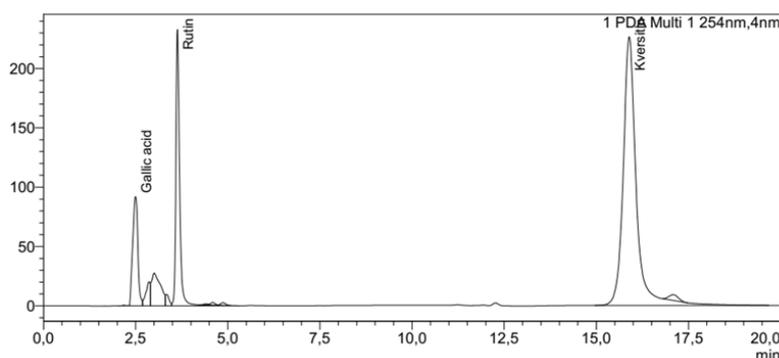


Figure 2.2. Chromatogram of gallic acid, rutin, and quercetin standard solutions.

From the chromatogram obtained with standard solutions of gallic acid, rutin, and quercetin (Figure 2.2), it can be seen that these compounds give specific peaks at 2.49, 3.63, and 15.89 minutes, respectively.

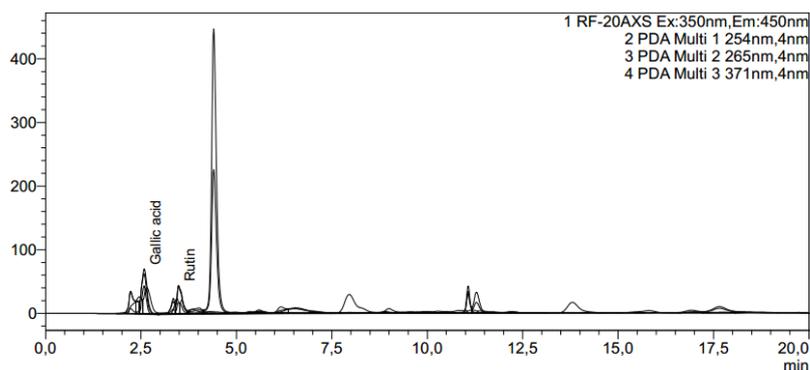


Figure 2.3. Chromatogram of saffron crocus extract.

In the chromatogram images of saffron florets extract (Figures 2, 3), peaks characteristic of gallic acid and rutin compounds can be seen at 2.49 and 3.63 minutes. There is no peak characteristic of quercetin. The table below the chromatogram shows that the concentrations of gallic acid and rutin in saffron extract are 0.04 and 0.014 mg/ml, respectively.

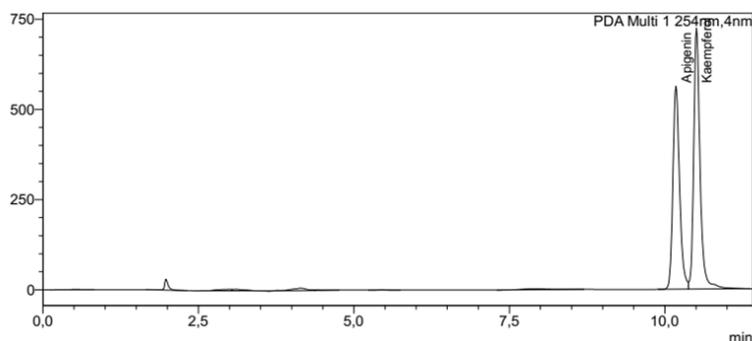


Figure 2.4. Chromatogram of apigenin and kaempferol standard solutions.

From the chromatograms of apigenin and kaempferol standard solutions (Figures 2.4), it can be seen that these compounds give specific peaks at 10.17 and 10.5 minutes, respectively.

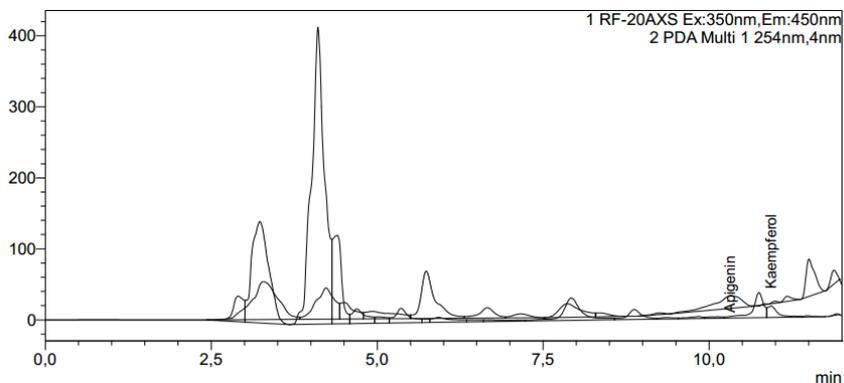


Figure 2.5. Chromatogram of saffron crocus extract.

the saffron florets extract (Figure 2.5), peaks characteristic of apigenin and kaempferol compounds can be seen at 10.134 and 10.75 minutes. The table below the chromatogram shows that the concentrations of apigenin and kaempferol in saffron extract are 0.04 and 0.014 mg/ml, respectively.

The content of some flavonoids in saffron crocuses is listed in the table below.

Table 2.4.

Results of determination of some flavonoids in saffron crocus extract by high-performance liquid chromatography

Names	Holding time, min.	Concentration, mg/ml	Quantity, mg/g
Gallic acid	2,493	0.04	1.6
Routine	3,635	0.014	0.56
Apigenin	10,178	0.001	0.04
Kaempferol	10,508	0.01	0.4

Table 2.4. represent the amount of substances (mg) in 1 gram of dry mass of saffron crocuses.

in Figures 2.3 and 2.5 above show that the concentrations of gallic acid, rutin, apigenin and kaempferol in saffron extract are 0.04 mg/ml, 0.014 mg/ml, 0.001 mg/ml and 0.01 mg/ml, respectively. From this, it is possible to determine the weights of the compounds being determined in 1 gram of saffron inflorescences, taking into account that the volume of the extract is 20 milliliters and the mass of the saffron inflorescence taken for analysis is 0.5 g.

Flavonoids are an important class of natural biologically active products. In particular, they belong to the class of plant secondary metabolites with a polyphenol structure, which are widely distributed in fruits, vegetables and some beverages. They have diverse biochemical and antioxidant effects that have been linked to various diseases such as cancer, Alzheimer's disease, atherosclerosis, etc. [160; pp. 1-15].

Gallic acid, rutin, quercetin, apigenin, and kaempferol are phenolic and flavonoid compounds, and in addition to the use of these compounds and their derivatives in the food industry as flavoring agents and preservatives, there is diverse scientific evidence in the literature about the biological and pharmacological activities of these phytochemicals, such as antioxidant, antimicrobial, anti-inflammatory, anticancer, antidiabetic, cardioprotective, gastroprotective, and neuroprotective effects [161; pp. 37-42].

In recent years, studies have shown that natural flavonoids can safely and effectively prevent and treat type 2 diabetes and its complications. Scientists have found that flavonoids can prevent diabetes by regulating glucose and lipid

metabolism, luteolin can improve diabetic cardiomyopathy by suppressing inflammation, kaempferol can reduce diabetic nephropathy by its antioxidant effect, puerarin can regulate blood glucose by inhibiting gluconeogenesis, and rutin has significant hypoglycemic effects and can increase insulin sensitivity [162;].

#### **§ 2.4. Determination of antioxidant activities of mixtures prepared from saffron crocus and flax seeds**

Antioxidants are substances such as vitamins, minerals, carotenoids, and polyphenols that play a very important role in the body's defense system against reactive oxygen species. The main function of antioxidants is to prevent oxidation in various situations, and studies have shown that they provide the best protection against the development of diseases caused by oxidative stress, such as cancer, cardiovascular disease, obesity, type 2 diabetes, hypertension, and cataracts [163; pp. 1328-1331].

The literature as a good antioxidant. We decided to add flaxseed to our saffron-based food supplement to achieve even better antioxidant activity.

In this study, we determined the antioxidant activities of several samples prepared from saffron crocus. For this, we prepared mixtures of saffron crocus and ground flax seeds in different mass ratios, which were given the conditional names ZF-1, ZF-2, ZF-3, ZF-4 (Table 2.5.).

Table 2.5.

Composition of samples		
Conditional name of the sample	Saffron flower buds	Flaxseed
ZF-1	100%	-
ZF-2	3	1
ZF-3	1	1
ZF-4	1	3

Saffron flowers morning at dawn gather taken and sun light unfallen under the circumstances from flowers stilts separate Freshly picked saffron florets were stored under good storage conditions, with low temperature and moderate air flow. In order to preserve the color, morphological characteristics, bioactive components

of saffron and to prevent biochemical and enzymatic changes in this process, it was dried in the traditional way, that is, at an average temperature of 35-45°C (Tables 2.6. to 2.9.).

Table 2.6.

Antioxidant activity of ZF-1 sample prepared from saffron crocuses

No.	ZF-1 concentration	Optical density of the control solution, D	experimental solution, D	Antioxidant capacity, %
1	100 mcg/ml	0.2017	0.1761	12.69
2	250 mcg/ml	0.3442	0.2870	16.60
3	500 mcg/ml	0.3604	0.2969	19.44
4	750 mcg/ml	0.3484	0.2836	18.57
5	1000 mcg/ml	0.4811	0.3750	22.05

Table 2.7.

Antioxidant activity of ZF-2 sample prepared from saffron crocuses

No.	ZF-2 concentration	Optical density of the control solution, D	experimental solution, D	Antioxidant capacity, %
1	100 mcg/ml	0.3001	0.2480	17.33
2	250 mcg/ml	0.3511	0.2872	18,19
3	500 mcg/ml	0.4619	0.3544	19.27
4	750 mcg/ml	0.3824	0.3030	20.76
5	1000 mcg/ml	0.3188	0.2624	21.70

Table 2.8.

Antioxidant activity of ZF-3 sample prepared from saffron crocuses

No.	ZF-3 concentration	Optical density of the control solution, D	experimental solution, D	Antioxidant capacity, %
1	100 mcg/ml	0.1917	0.1650	13.92
2	250 mcg/ml	0.2098	0.1774	15.44
3	500 mcg/ml	0.2276	0.1831	19.56
4	750 mcg/ml	0.2463	0.1959	20.46
5	1000 mcg/ml	0.2607	0.2033	22.01

Table 2.9.

Antioxidant activity of ZF-4 sample prepared from saffron crocuses

No.	ZF-4 concentration	Optical density of the control solution, D	experimental solution, D	Antioxidant capacity, %
1	100 mcg/ml	0.1917	0.1570	18.10
2	250 mcg/ml	0.2098	0.1664	20.68
3	500 mcg/ml	0.2276	0.1785	21.57
4	750 mcg/ml	0.2463	0.1898	22.97
5	1000 mcg/ml	0.2607	0.2001	23,24
	Gliclazide			10.0%
	Quercetin			37.4%

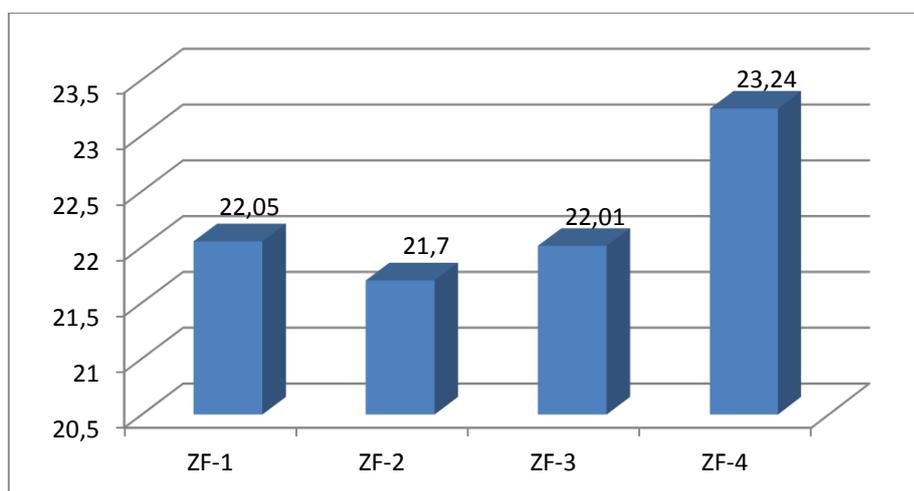


Figure 2.6. Antioxidant activity of samples prepared from saffron crocuses

The antioxidant activity of the samples was determined by the inhibition of the autooxidation reaction of adrenaline *in vitro* and the prevention of the formation of free oxygen species. The samples ZF-1, ZF-2, ZF-3, ZF-4 were compared with the standard antioxidant quercetin and gliclazide antioxidants, the results indicate the presence of antioxidant properties of the obtained samples.

From the above tables, it is clear that among the various saffron-based samples, the sample named ZF-4, prepared from saffron florets and flax seeds in a 1:3 mass ratio, has the highest antioxidant activity.

Due to the fact that the ZF-4 sample has a higher antioxidant activity than other samples, we selected it as the most suitable sample for the preparation of a food additive and named it «ASQAND».

## § 2.5. Determination of antiradical activity of the medicinal food supplements «ASQAND» and «ASUK»

Antioxidants may have different mechanisms of action, and it is recommended to study their activity using different methods [164; p. 41].

The DFPG assay method is based on the reduction of the stable free radical 2,2-Diphenyl-1-picrylhydrazyl by the action of medicinal substances, extracts, or other biological sources that can act as hydrogen donors, and is a widely used, rapid, easy, and inexpensive approach [165].



Table 2.11

Time dependence of the antiradical activity of the medicinal food supplement “ASQAND”

Optical density , D	Time, minute	Concentration
0.1	30	0.11
0.2	27.5	0.16
0.3	25	0.20
0.4	22.5	0.28
0.5	20	0.30
0.6	17.5	0.40
0.7	15	0.48
0.8	12.5	0.53
0.9	10	0.64
1.0	7.5	0.72
1.1	5	0.80
1.2	2.5	0.97
1.3	0	1

The concentration of DFPG based on non-linear regression is 0.1 mM. Measurements were performed immediately after the addition of the tested extracts at 20°C. The concentration of the studied extracts was 50 µl/ml of the pre-prepared solution. The biologically active food supplement “ASQAND” was diluted 100 times with the appropriate solvents (water).

Experimental data show that the biologically active food supplement “ASQAND” has the ability to bind free radicals. To quantitatively assess the antiradical activity, we used the stable radical 2,2-diphenyl-1-picrylhydrazyl (DFPG), as well as the  $t_{50}$  indicator, the time required to reduce the initial concentration of the radical for the studied samples to 50% inhibition activity.

of DFPG with extracts at 20 ° C,  $t_{50}$  for the “ASQAND” medicinal food supplement was  $11.7 \pm 0.98$ , and when diluted 100 times, it was  $52.47 \pm 2.17$ , and for saffron it was  $29.9 \pm 0.69$ , and when diluted 100 times, it was  $48.65 \pm 3.08$  (Table 2.12.).

Table 2.12.

50% inhibitory concentration ( $IC_{50}$ ) values and the time required to reduce the concentration of DFPG by 50% ( $t_{50}$ ) when reacting with the tested extracts . (n=5)

Samples	$IC_{50}$ , µl	$t_{50}$ , sec 50 µl substance
Saffron	$29.9 \pm 0.69$	$67.4 \pm 3.45$
Saffron ( diluted )	$48.65 \pm 3.08$	$57.49 \pm 2.97$
«ASKAND»	$11.7 \pm 0.98$	$11.7 \pm 0.98$
«ASQAND» ( diluted )	$52.47 \pm 2.17$	$64.63 \pm 3.86$

Analysis of the experimental results obtained in the study of extracts showed that the “ASQAND” medicinal food supplement has a higher ARF than saffron crocuses.

As a result of a comparative analysis of the results of studies on the antiradical activity of various plants with medicinal properties, the decoctions of which are widely used in folk medicine, using the DFPG method, it was found that the antiradical activity of the “ASQAND” medicinal food supplement is significantly higher (Table 2.13) [167; pp. 523-526, 168; pp. 2680-2690, 169; pp. 65-68].

Table 2.13.

Comparative analysis of ARF values (%) of the food supplement “ASQAND” and various medicinal plants

Samples	«ASQAND»	Na'matak	Turmeric	Deer grass
ARF values (%)	88.3	87.78	71.64	34.11

The above information is taken from literature sources. According to these sources, a solution of ascorbic acid in ethanol was taken as a standard solution in studies, and its ARF value was shown to be 90% [ 170; pp. 1337-1356].

In order to develop a medicinal food supplement based on olive oil, we determined and compared the antiradical activities of solutions of samples prepared by mixing olive oil and flaxseed oil, which has high medicinal properties, in ethyl acetate at a concentration of 50 µl/ml (Table 2.14.).

Table 2.14.

Composition and antiradical activity of mixtures of olive and flaxseed oils in different proportions

Conditional name of the sample	Sample composition (%)		Antiradical activity (%)
	Olive oil	Flaxseed oil	
ZN-1	100	-	33.64±2.2
ZN-2	75	25	40±1.8
ZN-3	50	50	34.45±2.6
ZN-4	25	75	32.74±1.6

Above cited in the table to the information based on examples between olive and 3:1 volume ratio of flax proportional mixture was named ZN -2 is the most high anti-radical to activity has that it is understanding possible. Therefore for also olive and flax 3:1 volume ratio of oils in proportion taken this ZN -2 na‘munasini

food - food addition for acceptable this is it as selectively taken and “ASUK” name was given .

Continuing our research on determining the antiradical activity of food additives, the antiradical activity of the olive oil-based medicinal food additive "ASUK" was determined using the 2,2-diphenyl-1-picrylhydrazyl (DFPG) free radical inactivation method.

In this study, we examined the effect of increasing the concentration of the “ASUK” medicinal food supplement on antiradical activity. For this purpose, solutions in ethyl acetate with concentrations of 25  $\mu\text{l/ml}$ , 50  $\mu\text{l/ml}$ , 75  $\mu\text{l/ml}$  and 100  $\mu\text{l/ml}$  were taken for testing. When the studied samples were added to the ethyl acetate solution of DFPG, the free radical molecules were converted to a non-radical form, and the intensely purple solution of DFPG became colorless [171].

The dynamics of the decrease in the optical density of the DFPG solution of the samples is shown below.

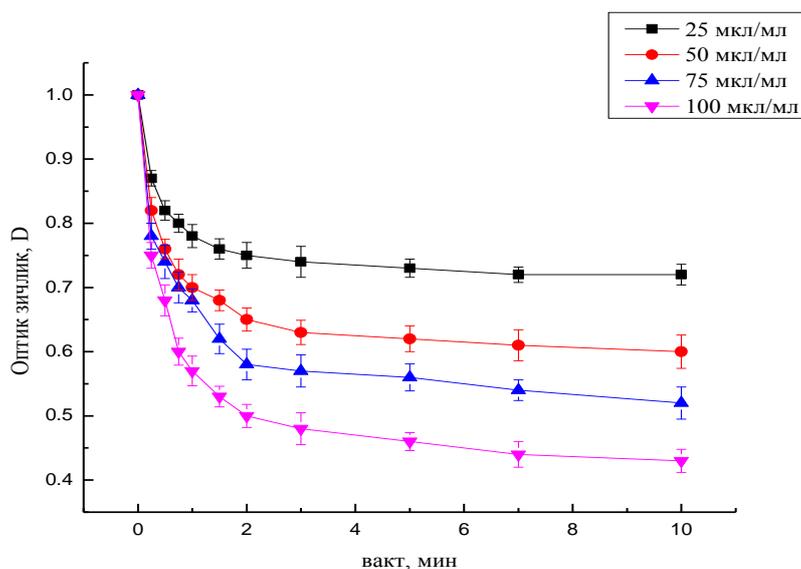


Figure 2.8. Effect of “ASUK” samples with different concentrations on the optical density of DFPG solution.

The table below shows the coefficients of reduction in the optical density of DFPG solution of solutions of various concentrations of the “ASUK” medicinal food supplement, expressed in numbers (%) depending on the ability of the samples to inhibit DFPG molecules (Table 2.15.).

Table 2.15.

Effect of different concentrations of “ASUK” samples on the level of inhibition of DFPG solution (n=5)

Example	Inhibition, % ( at 10th minute )			
	25 µl / ml	50 µl / ml	75 µl / ml	100 µl / ml
“ASUK” food supplement	28 ±2.1	40 ±1.8	48 ±1.4	57 ±2.4

ASUK healer food - food addition concentration increased yellow his/her anti-radical activity also increasing to go our view possible.

By comparing the results of studies on the antiradical activity of vegetable oils using the DFPG method, it can be concluded that the antiradical activity of the “ASUK” medicinal food supplement is significantly higher [172; p. 17-27, 173; 174; p. 409-413.].

Table 2.16.

“ASUK” food addition and different oils ARF values comparative analytical (%)

Samples	«ASUK»	Sesame oil	Grape seed oil	Olive oil	Flaxseed oil
ARF value (%)	57 ±2 . 4	46.1 ± 3.1	49.03 ± 0.53	20; 66	74.7

The results in Figure 2.8 and Table 2.20 above show that the “ASUK” medicinal food supplement exhibits high antiradical activity.

## **§ 2.6. Results of determining the effect of the medicinal food supplement “ASQAND” on the body’s oxygen consumption in conditions of hypoxia**

Sugary diabetes and heart blood vessel between diseases close dependency there is be, this diabetes with sick in patients disease and the science of the most wide widespread obesity, hypertension and dyslipidemia such as heart - blood vein danger factors sugary diabetes with sick in patients wide widespread to be , them heart diseases the risk increases [175; 1246-1258- p .].

In many countries, heart attacks, strokes, and cancer have become the most common causes of death. The causes of these diseases are many and varied, including genetic predisposition and environmental influences, but they all have a common feature, since the development of these pathological conditions leads to a limitation of the amount of oxygen. At the same time, cells and organisms can trigger adaptive responses to hypoxic conditions, which help them overcome these threatening conditions [176; pp. 1875–1882].

Scientific evidence, which is being studied and developed by researchers, shows that several cells and tissues in the body of patients with diabetes mellitus, including the retina, kidney, pancreatic islets, and skin, are in a hypoxic state, and hypoxia plays an important role in the further aggravation of diabetes mellitus and its complications [177;].

Scientists emphasize the existence of complex adaptive mechanisms that contribute to cell survival during hypoxia, such as metabolic reprogramming of oxidative phosphorylation in mitochondria to anaerobic glycolysis, increased erythropoiesis and angiogenesis, and proliferation [178; pp. 709-716].

In this part of our research, we studied the effect of the medicinal food supplement “ASQAND” on the body’s oxygen consumption in conditions of hypoxia.

The results showed that the standard metabolism in animals decreased under the influence of the samples and this process increased in proportion to the increase in the amount of samples . If the samples were administered to rats at 16, 32, 48, 64 and 80 mg/kg and measured 60 minutes later, the standard metabolism decreased by 15.1; 24.2; 33.3; 41.6 and 60.6% (Table 2.17.).

Table 2.17.  
of the medicinal food supplement “ASQAND” on oxygen consumption (M±m; n = 6).

Sample size , mg /kg	Rat	
	Oxygen consumption, mM O <sub>2</sub> /minkg	
0	13 72 ±1 40	100
16	1 165 ±1 36 *	84.9
32	1040 ± 130 ***	75.8
48	915 ± 124 ****	66.7
64	801 ± 8 2 ****	58.4
80	540 ± 67 ****	39.4

Note: the level of confidence here is defined as follows:

\* R < 0.05; \*\* R < 0.02; \*\*\* R < 0.01; \*\*\*\* R < 0.001.

Thus, the “ASQAND” medical food supplement significantly reduces the transport of oxygen to the body, which depends on the rhythm of heart contractions, minute blood volume and oxygen capacity of the blood. It switches from an active metabolic state to a passive metabolic state. From this, the “ASQAND” medical food supplement The effect at the organism level is

manifested by reducing energy and nutrient consumption, that is, by shifting oxygen and substrates to a more economical consumption system.

### **§ 2.7. Results of determining the effect of the medicinal food supplement “ASQAND” on the peroxide oxidation process**

In the study of the physicochemical properties and physiological state of the mitochondrial membrane in normal and pathological conditions, it has been shown that the study of the permeability of the mitochondrial membrane to various ions and the processes of lipid peroxidation is of great practical importance. Because changes in the antioxidant system in mitochondria, in turn, lead to changes in the antioxidant system in cells and tissues. As a result, as a result of membrane dysfunction, oxidative phosphorylation processes in mitochondria change and the balance of free radical formation is disturbed [179;].

It should also be noted that under normal physiological conditions, LPO processes do indeed occur in cells. During the course of LPO processes in cells, ions with variable valence, organic hydroperoxides, etc., which are its inducers, are activated. In biological fluids and cells, there is a certain amount of iron ions with variable valence, which create conditions for the formation of cytotoxic radicals of lipids in cells. The amount of free radicals in metabolic processes in organs and tissues varies greatly, and this plays an important role in the processes of energy metabolism in the cell [180; p. 71].

Therefore, iron ions are used in the study of LPO processes. This is one of the main test systems in the study of the antioxidant properties of various biologically active substances. In addition, it has been shown that the induction of LPO processes without calcium ions leads to the activation of all phospholipases located in the mitochondrial membrane. It is known from the literature that in normal cellular activity, the oxidation of substrates in the presence of oxygen results in the formation of 98% of ATP and 2% of reactive oxygen species. In pathological conditions, this balance is disturbed due to the increase in free radicals [181].

are crucial in highlighting the pathological role of oxidative stress in the development of type 2 diabetes. [182].

The following is a summary of the inhibitory effect of the “ASQAND” medicinal food supplement on Fe<sup>2+</sup>/ascorbate-induced mitochondrial dysfunction in *in vitro* experiments (Figure 2.9).

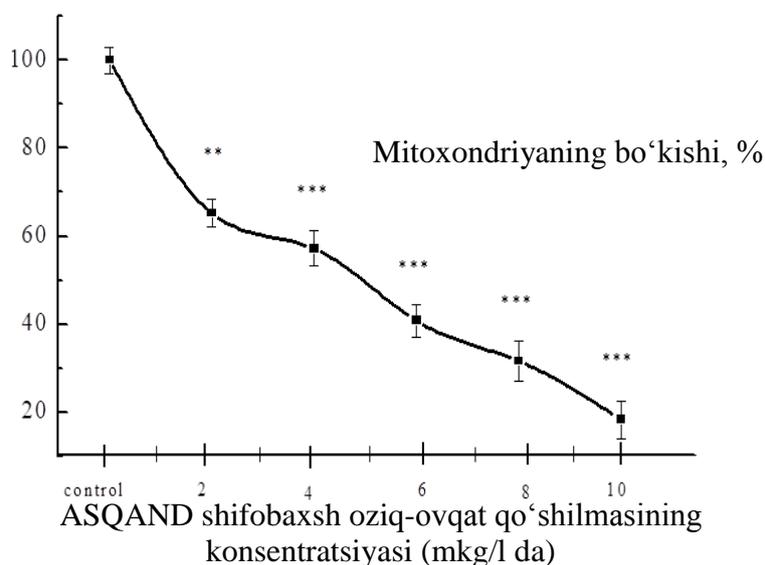


Figure 2.9. Effect of the medicinal food supplement “ASQAND” on the process of peroxidative oxidation of lipids in mitochondria induced by Fe<sup>2+</sup>/ascorbate .

Note: The ordinate axis shows the mitochondrial swelling under the influence of Fe<sup>2+</sup>/ascorbate, the abscissa axis shows the applied concentrations of the medicinal food supplement “ASQAND” . Incubation medium - 125 mM KCl, 10 mM tris-HCl, pH 7.4. (\*\* P<0.01, \*\*\* P<0.001; n=4).

Fe<sup>2+</sup>/ascorbate to the incubation medium causes a sharp increase in the process of lipid peroxidation in mitochondria. It is known that under the influence of the Fe<sup>2+</sup>/ascorbate system, mitochondria swell and their size increases. In this case, the variability of the mitochondrial membrane increases, and the mitochondrial membrane potential decreases. By influencing the LPO process induced by the Fe<sup>2+</sup>/ascorbate system with different concentrations, it was found that kaempferol has membrane-active properties [183].

During the peroxidation processes of lipids in mitochondrial membranes, ion channels in the membrane are disrupted, allowing various ions and free radicals to enter and accumulate. 2, 4, 6, 8, 10 of the “ASQAND” medical food supplement It

was found that under the influence of solutions with a concentration of 1000 µg/l , the mitochondrial depletion phenomenon was reduced by 36, 43, 60, 68, 80%, respectively. The main reason for this is that flavonoids exhibit antioxidant properties and carry out the process of free radical scavenging. In this study, the antioxidant properties of the “ASQAND” medicinal food supplement prepared on the basis of saffron crocus were examined.

### **2.8-§. Results of determining the toxicity level of the medicinal food supplement “ASQAND”**

and Wilcoxon method was used to determine acute toxicity parameters. The feed was administered orally in the form of a 4% solution at doses of 200, 400, 800, 900 and 1000 mg/kg. On the first day of the experiment, the condition of the animals was monitored every hour in laboratory conditions. During the experiment, survival rate, general condition, possible tremors and death were considered as indicators of their functional state [184;].

Subsequently, the general condition and activity of the animals in all groups, individual behavioral states, respiratory depth and rate, fur and skin condition, urinary frequency, and body weight changes were monitored daily for 2 weeks in the vivarium. All animals were kept in the same vivarium under a common diet, with no restrictions on water or food.

“ASQAND” medicinal food supplement, the effects of acute poisoning in the above-mentioned parameters of animals were not observed. During the entire experiment, no animal deaths were recorded at these doses. When the “ASQAND” medicinal food supplement was administered orally once at a dose of 800 mg/kg, 16.6% of animals died. When administered at a dose of 900 mg/kg, 50% of animals died. When administered at a dose of 1000 mg/kg, 83.3% of animals died. Based on the results obtained, it was determined that the average lethal dose (LD<sub>50</sub>) of the “ASQAND” medicinal food supplement when administered orally once was 870 mg/kg. The results obtained are presented in Table 2.18.

Table 2.18.

Animal type	Gender	Doses mg/kg	Number of dead animals in the group	LD <sub>16</sub>	LD <sub>50</sub> with confidence interval	LD <sub>84</sub>
Mouse	male	2 00	6/0	≥ 700mg/kg	≥ 870mg/kg	≥ 1 100mg/ kg
		4 00	6/0			
		8 00	6/ 1			
		9 00	6/ 3			
		1,000	6/ 5			

Thus, the results of the study of the acute toxicity of the medicinal food supplement "ASQAND" showed that this drug belongs to class IV low-toxic substances [185; 5-12-p.] and the median lethal dose (LD<sub>50</sub>) after a single oral administration is 870 mg/kg.

### § 2.9. Results of the evaluation of the anti-diabetic effect of the medicinal food supplement "ASQAND"

Hyperglycemia-induced oxidative stress triggers mechanisms that damage  $\beta$ -cells, resulting in the accelerated development of diabetes. These results indicate the formation of the DM model. Against the background of DM, activation of gluconeogenesis, an increase in glucose content as a result of glycogen breakdown in the liver, and a decrease in protein content are observed. Glucose is the main energy substrate for the organism to survive under normal conditions. Maintaining the normal level of glucose in the blood is ensured by the occurrence of two processes: the rate of glucose formation by glycogenesis and gluconeogenesis, and the rate of glucose breakdown in the tissues and cells of the body. Naturally, the level of glucose in the blood significantly affects these processes. In erythrocytes, glucose participates in the pentophosphate reactions, which is an oxidation step that ensures the formation of the NADF coenzyme necessary for the reduction of glutathione [186; pp. 107-113].

Table 2.19.

No.	Groups	n	Separated Time	after the QD was called (last day)
1	Intact group	4	271±6.78	282±4.52

2	Diabetes group	4	2 7 3±7.04	2 5 7±5.67*
3	Diabetes +diabeton	4	2 8 2±5.48	2 75 ±5.78
4	Diabetes+“ASKAND”	4	2 8 0±6.17	2 74 ±6.62 *

Note: – statistical analysis shows the difference in variability between the control and AD+drug groups \* p <0.05

n – number of experimental rats;

Intact group – healthy experimental rats that were not diabetic;

Before the experimental diabetes model was induced (Table 2.19.), all male rats were selected and their weights were measured. After the DM model was induced, the animals’ weights were measured, and it was found that the diabetic model animals had slightly lost weight, which is due to the toxic effects of alloxan. The animals’ weight loss was accompanied by excessive urine excretion, which indicates that this was diabetes.

Table 2.20.

Changes in glucose levels in experimental diabetes model rats (mmol/l)

No.	Groups	n	Days			
			1	1 5	21	28
1	Intact group	4	4.5± 0.45	4.8± 0.54	4.8±0.23	4.8± 0.52
2	Diabetes group	4	4.7± 0.82	12.9± 0.87	13. 3 ±0.57*	13. 5 ± 0.74
3	Diabetes+diabeton	4	5.0± 0.5 1	12.3± 0.95	10.9±0.82	7.0 ± 0.97
4	Diabetes+“ASKAND”	4	4.7± 0.68	12.7± 0.95	1 0 .7±0.45*	6.9 ± 0.88

Before model call (day 1 ) , After model call ( day 1-5 ), After drug administration ( days 21 and 28 )

Note: – statistical analysis shows the difference in variability between the control and AD+drug groups \* p <0.05

Initially, after chronic alloxan administration in animals , glucose levels increase sharply, and animals experience dramatic changes, including weight loss, polyuria, hypodynamia, and cognitive changes (Table 2.20.). No dramatic changes were observed in intact and control groups, but experiments showed that glucose levels decreased when given to AD+drug groups for 8 days, and the “ASQAND” therapeutic food supplement had an effect.

Table 2.21.

Glycogen content in liver and muscle tissues under experimental diabetes				
No.	Groups	n	Liver	Muscle
			mg %	
1	Intact group	4	1324.5 ± 5.55	217.64 ± 3.18
2	Diabetes group	4	980.33 ± 4.41	229.36 ± 8.71 *
3	Diabetes + diabeton	4	1126.59 ± 5.48	221.97 ± 6.77 *
4	Diabetes+»ASQAND»	4	1211.31 ± 6.12	220.26 ± 4.43 *

Shows the difference in variability between the control and AD+drug groups \* p <0.05;

Erythrocytes are considered the most convenient model in which it is possible to observe the process of destruction, the restoration of important structures that support the vital activity and integrity of the cell, since protein synthesis cannot occur in them (Table 2.21.). Erythrocytes do not have mitochondria, therefore they use glucose as an energy source. 90% of the incoming glucose is normally consumed by anaerobic glycolysis, and the remaining 10% is spent on the pentophosphate pathway [187; 141-147-p., 188; 328-329-p. ]

Glycosylated hemoglobin (glycated hemoglobin A1c, %HbA1c) determines the level of Hb in the blood over a long period (up to 3 months). This type of Hb is formed as a result of a slow process between Hb and glucose in the blood serum (this process occurs spontaneously, i.e. without the participation of enzymes). The glycosylation of Hb and its amount depend on the average amount of glucose during the entire life of the erythrocyte. Of the three types of glycosylated Hb, HbA1a, HbA1b, HbA1c, only the latter HbA1c allows us to draw conclusions about the presence and degree of diabetes mellitus [189; p. 59.]

When AD model animals were given antioxidant drugs, the amount of glycosylated Hb in the blood of experimental diabetic animals increased by 1.6 times compared to the intact group. However, it was found that the amount of HbA1c decreased after treatment with antioxidant drugs. The main reasons for the increase in HbA1c in AD model animals can be explained by the decrease in the activity of the enzyme glucose-6-phosphate dehydrogenase and the occurrence of hemoglobinopathy. AD rats showed a 1.6-fold increase in HbA1c compared to intact animals and a decrease in hemoglobin.

Table 2.22.

Glycated hemoglobin and hemoglobin content in experimental diabetic blood.

No.	Groups	n	Glycated hemoglobin % HbA <sub>1c</sub>	Hemoglobin g/dl
1	Intact group	4	4.5±0.29	12.75±0.85
2	Diabetes group	4	7.85±0.47	9.85±0.90 *
3	Diabetes+ diabeton	4	6.17±0.68	11.25±0.81 **
4	Diabetes+“ASKAND”	4	6.11±0.52	11.12±0.97 **

Note: – statistical analysis shows the difference in variability between the control and AD+drug groups \* p <0.05; \*\* p <0.01

In this study, we studied the effect of the “ASQAND” medical food supplement on indicators such as body weight changes, blood sugar levels, glycogen levels in the liver and muscles, and glycosylated and non-glycosylated hemoglobin levels in the blood associated with diabetes mellitus (Table 2.22.).

The results show that 6% of the rats in the Diabetes group lost weight during the study. This figure was 2.5% in the Diabetes+Diabeton group, and 2.1% in the Diabetes + ASQAND group.

It can be seen that the blood sugar level in the Diabetes group increased continuously on days 15, 21 and 28, while it decreased in the Diabetes+drug groups. This was especially evident in the Diabetes + “ASQAND” group. The blood sugar level in the Diabetes+ “ASQAND” group rats by day 28 was almost twice lower than in the Diabetes group, and 1.5% lower than in the Diabetes+diabetone group.

The amount of glycogen in the liver and muscles also showed better results in the Diabetes + “ASQAND” group compared to the other groups, according to the k indicator.

that the level of glycosylated hemoglobin in the blood of experimental rats was also lower in the Diabetes + “ASQAND” group than in the Diabetes group and the Dabet+diabeton groups. “ASQAND” Experiments have shown that the desired results can be achieved through the continuous use of a medicinal food supplement.

## **2.10-§. Results of evaluation of the anti-inflammatory and antioxidant properties of the medicinal food supplement “ASUK”**

This phase of the research was aimed at studying the effect of the food additive “ASUK” on various components of inflammation. The first step of the research was to evaluate the AEF of the food additive “ASUK” and glycerol in a carrageenan edema model [190; p. 944].

Carrageenan-induced acute exudative inflammation was observed in rats at 3 and 24 hours after phlogogen administration. As shown in Table 2.23, the maximum edema in control rats occurred after 3 hours, with the paw volume increasing by  $93.8 \pm 4.6\%$  compared to the initial value, and after 24 hours the edema  $\pm$ decreased to  $50.0 \pm 6.5\%$ .

Similar dynamics were observed in the groups that received the food additive “ASUK” and glycerin through a gavage, but in this case the degree of edema was smaller. Thus, 3 hours after the administration of carrageenan to rats that received the food additive “ASUK” in doses of 0.25 and 0.5 ml, the edema in the paws of their rats was  $44.1 \pm 6.80\%$  and  $26.3 \pm 4.07\%$  ( $p < 0.05$ ), and after 24 hours it was  $20.5 \pm 6.82\%$  and  $12.8 \pm 2.75\%$ , respectively.

Compared to control animals, the AEF “ASUK” food additive, 3 and 24 hours after the introduction of carrageenan at a dose of 0.25 ml, was 53.0 and 59.0%; at a dose of 0.5 ml, it was 72.0 and 74.4%.

In the experiment, in rats that received glycerol in doses of 0.25 and 0.5 ml, the tumor size was  $65.1 \pm 17.0$  and  $53.3 \pm 14.3\%$  ( $p < 0.05$ ) 3 hours after carrageenan injection, while after 24 hours the tumor decreased by  $22.4 \pm 2.47\%$  ( $p < 0.01$ ) and  $17.4 \pm 3.75\%$ , respectively, with all indicators being statistically significantly lower than the control (Table 2.23.).

Table 2.23.

of “ASUK” food additive and glycerin on the course of carrageenan-induced inflammation in rats ( $M \pm m$ ;  $n=6$ )

Groups	Dose, mg/kg	After 3 hours		24 hours	
		Of the tumor size, %	AE F, %	Tumor size, %, AEF, %	AEF, %
Control	-	93.8 $\pm$ 4.60	-	50.0 $\pm$ 6.5	-
Glycerin	0.25 ml	65.1 $\pm$ 17.0	31, 0	22.4 $\pm$ 2.47 ***	55.2
	0.5 ml	53.3 $\pm$ 14.3 **	43.2	17.4 $\pm$ 3.75**	65.2
“ASUK”	0.25 ml	44.1 $\pm$ 6.80***	53.0	20.5 $\pm$ 6.82	59.0
	0.5 ml	26.3 $\pm$ 4.07 **	72.0	12.8 $\pm$ 2.75***	74.4

Note : \* -  $p < 0.05$ , \*\* -  $p < 0.01$ , \*\*\* -  $p < 0.001$  compared to control.

The results show that the food additive “ASUK” The activity of glycerin activity, but without statistically significant differences. At the same time, these results are consistent with those of other researchers. Analytical reviews of the carrageenan edema model have reported that rat paw enlargement can reach 66-180% and that edema development reaches its maximum after 3-5 hours.

Thus, the study of the antiexudative effect of the food additive «ASUK» in inflammatory conditions showed that this drug was more effective than glycerin at all doses studied.

The second phase of the study is the food supplement “ASUK” and glycerol in a “cotton granuloma” model, which allows for the assessment of their anti-exudation and anti-proliferative effects [191;].

The results obtained showed that the “ASUK” food supplement reduced the level of exudation, this indicator was 346.0 $\pm$ 29.4 mg in the control, 228.0 $\pm$ 22.4 mg ( $p < 0.05$ ) in the “ASUK” food supplement at a dose of 0.25 ml ; and 206.9 $\pm$ 21.3 mg at a dose of 0.5 ml, respectively (Table 2.24.).

A decrease in the degree of proliferation inhibition and a decrease in the mass of granulation fibrosis tissue were observed in the mass of cotton balls when measured: they were 86.5 $\pm$ 9.70 mg in the control , and 55.8 $\pm$ 7.4 and 53.8 $\pm$ 6.3 mg

( $r < 0.05$ ) in the doses of 0.25 and 0.5 ml of the “ASUK” food additive, respectively.

When the above doses of the food additive “ASUK” were administered, the suppression of exudative processes increased to 34.1 and 40.2%, and proliferative processes to 35.5 and 37.8%, respectively, compared to the animals in the control group. At the same time, the indicators of the decrease in the mass of exudative and granulation fibrous tissue were statistically significantly higher than the control by 1.5 and more. The indicator of the reduction in the level of exudation in glycerol was  $243.3 \pm 23.3$  mg at a dose of 0.25 ml ( $p < 0.05$ );  $250.0 \pm 35.4$  mg at a dose of 0.5 ml, respectively. A decrease in the degree of suppression of proliferation and a decrease in the mass of granulation fibrosis tissue were observed in the mass of cotton balls when measured: at doses of 0.25 and 0.5 ml, the values were  $62.2 \pm 6.98$  and  $60.0 \pm 5.96$  mg ( $p < 0.05$ ), respectively.

Table 2.24.  
of the anti-inflammatory activity of the food additive “ASUK” and glycerin in the “cotton granuloma” model in rats ( $M \pm m$ ;  $n=6$ )

Groups	Dose (mg/kg)	EM, mg	E B, %	GM, mg	P B, %
Control	-	$346.0 \pm 29.4$	-	$86.5 \pm 9.70$	-
Glycerin	0.25	$250.0 \pm 35.4$	27.7	$62.2 \pm 6.98$	28.1
	0.5	$243.3 \pm 23.3^*$	29.7	$60.0 \pm 5.96$	30.6
«ASUK»	0.25	$228.0 \pm 22.4^*$	34.1	$55.8 \pm 7.4^*$	35.5
	0.5	$206.9 \pm 21.3$	40.2	$53.8 \pm 6.3$	37.8

Note : \* -  $p < 0.05$ , \*\* compared to control.

When the above doses of glycerol were administered, the suppression of exudative processes increased to 27.7 and 29.7%, and proliferative processes to 28.1 and 30.6%, respectively, compared to animals in the control group.

Thus, the study of the effect of the “ASUK” food additive in the “cotton granuloma” model showed that it was more effective than glycerol at all doses studied in an environment with pronounced proliferative processes .

the past decade have demonstrated a clear link between oxidative stress and systemic inflammation. Future studies may help to guide the search for ways to suppress the excessive generation of reactive oxygen species, to reduce the level of

exposure to damaging factors, and to find pharmacological agents that can inhibit the pathological activity of free radicals and, consequently, oxidative stress. In this regard, antioxidants have been shown to have high anti-inflammatory activity.

### **Conclusions on Chapter II**

The following conclusions were drawn by analyzing the results of experiments conducted to determine the biological activity of olive oil and saffron crocus, the objects of the study, and the amount of biologically active substances and micro- and macroelements in their content:

1. When examining the content of macro and microbiological elements in saffron crocuses using modern physicochemical methods, it was found that per 100 g of dry product it contains 160.3 mg of magnesium, 74.325 mg of zinc and 1.025 mg of copper. This increases the importance of saffron crocuses in diabetes mellitus, which store ions of these metals, which act as cofactors for enzyme systems involved in carbohydrate metabolism in the body;

When the concentration of  $\beta$  -carotene in saffron crocuses was tested using a spectrophotometric method, it was found that each gram contained 416  $\mu\text{g}$  of  $\beta$  -carotene.  $\beta$  -carotene reliably protects the body of patients with diabetes from the harmful effects of reactive oxygen species;

3. When analyzing the content of phenolic and flavonoid compounds such as gallic acid, rutin, apigenin and kaempferol in saffron florets using the YSSX method, it was determined that these compounds were present in saffron florets. The analysis showed that gallic acid-1.6 mg%, rutin-0.56 mg%, apigenin-0.04 mg% and kaempferol-0.4 mg %. The presence of flavonoids in saffron crocuses suggests that it contributes to increasing insulin sensitivity;

4. When testing the antioxidant activity of samples prepared based on saffron crocus, it was found that the sample obtained from a mixture of saffron crocus and flax seeds in a ratio of 1:3 showed the highest result of 23.24%;

5. To quantitatively assess the antiradical activity of the obtained food additives, we found that they have high antiradical properties when evaluated against the stable radical 2,2-diphenyl-1-picrylhydrazyl (DFPG);

the medicinal food supplement “ASQAND” in the solution, obtained on the basis of saffron inflorescences, on reducing oxygen consumption under hypoxic conditions, thereby switching to a system of economical consumption of oxygen and substrates was studied.

The medicinal food supplement “ASQAND” based on saffron crocuses affects the process of lipid peroxidation and protects mitochondrial membranes.

Medicinal food supplement “ASQAND” based on saffron crocus was tested, and it was found that it belongs to class IV low-toxic compounds and the median lethal dose (LD<sub>50</sub>) after a single oral administration is 870 mg/kg.

medicinal food supplement “ASQAND” based on saffron crocus were evaluated in vivo. Its hypoglycemic properties were found to be more effective than the synthetic drug Diabeton;

10. When the anti-inflammatory activity of the olive oil-based medicinal food supplement “ASUK” was tested in vivo using the carrageenan swelling method, it was found to be 74.4% more effective than the control.

## **CHAPTER III. DETERMINATION OF THE CHEMICAL COMPOSITION OF SAFFRON FLOWERS AND OLIVE OIL USING PHYSICO-CHEMICAL METHODS AND EXPERIMENTAL STUDY OF THEIR BIOLOGICAL ACTIVITIES.**

### **3.1 -§. Determination of macro- and microelements in saffron florets by optical emission spectrometry**

For the purpose of analyzing the sample of saffron flower buds, it was first dried in a drying cabinet (VWR DRY-line, Germany) until the mass remained unchanged to dry the moisture content. For mineralization of the completely dried sample, i.e. to make it into a clear solution, 200 mg was weighed on an analytical balance (FA2204N). To mineralize the sample, a mineralization device (MILESTONE Ethos Easy, Italy). For this, a sample (200 mg), 6 ml of nitric acid (HNO<sub>3</sub>) purified by distillation, i.e. distilled acid in an infrared light-based acid purification device (Distillacid BSB-939-IR), and 2 ml of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) as an oxidant were placed in the test tube of the device. The whole mixture was mineralized at 180 °C for 20 min.

After the mineralization process was complete, the mixture in the test tube was transferred to a separate conical volumetric flask and diluted with distilled water to 25 ml.

The solution in the flask was placed in special test tubes in the autosampler section and placed for analysis. The prepared sample was sent to Avio for analysis. 200 (ICP – OES (Inductively Coupled Plasma Optical Emission Spectrometer) (Perkin Elmer, USA) The device has a high level of accuracy, allowing the measurement of elements in the solution to an accuracy of 10<sup>-9</sup> g [192; pp. 1870-1879].

### 3.2 -§. Determination of $\beta$ -carotene content in saffron florets by spectrophotometry

Saffron inflorescences were selected to determine the amount of  $\beta$ -carotene in the samples under laboratory conditions. Saffron for analysis (accurately weighed AF 2204 N, accuracy level 0.1  $\mu\text{g}$ ) 5 g was weighed, ground to a size of 1 mm in diameter and placed in a 100 ml volumetric flask. 25 ml of hexane was used as solvent ( $\text{C}_6\text{H}_{14}$  chemically pure, TU 2631-003-) was extracted. The extraction was carried out for 90 min in a magnetic stirrer (MSH-300 BIOSAN, Latvia). After the extraction process was completed, the solution was filtered. 1 ml of the filtrate was taken and placed in a 25 ml volumetric flask and diluted with solvent to the mark.

Carotene content was determined using a NACH LANGE DR 3900 (Germany) spectrophotometer (spectral wavelength range, 300–800 nm).

In parallel with the process of determining the amount of carotenoids, a 0.04% solution of potassium dichromate ( $\text{K}_2\text{Cr}_2\text{O}_7$ ) was prepared for comparison and its optical density was determined at a wavelength of 450 nm.

The optical density of a standard solution of potassium dichromate (DSt 4220 – 75 chem. pure) was measured in parallel with purified water (BIOSAN, Latvia).

The result was calculated using the formula: mg% of  $\beta$ -carotene in the total carotene content of saffron crocuses [151; pp. 139-144].

$$X = \frac{D_1 \cdot 0,00208 \cdot 25 \cdot 25 \cdot 100 \cdot 100}{D_0 \cdot m \cdot 1 \cdot (100-w)} \quad (3.1).$$

Where  $D_1$  is the optical density of the solution under investigation;

$D_0$  - optical density of a standard sample solution of potassium dichromate, corresponding to 0.00208 mg of  $\beta$ -carotene;

$m$  is the mass of the sample, g.

$w$  - moisture content in the sample, % (ISO 3632-2-93)

### 3.3 -§. Determination of some flavonoids in saffron crocuses using the HPLC method

The following method was used to quantitatively determine flavonoids in saffron flower buds.

To extract the analytes from the saffron sample, we used 96% ethyl alcohol as a solvent . For this, 0.5 grams of saffron sample was taken, mixed with 20 ml of alcohol and extracted using a magnetic stirrer for 75 minutes at 30°C. The stationary phase was an Agilent Zorbax 4.6 mm ID x 12.5 mm cartridge and a Perkin Elmer C18 250x4.6 mm 5 µm C<sub>18</sub> (USA) column to determine the amount of rutin, gallic acid and quercetin in the samples. For this purpose, solutions of 0.5% acetic acid solution and standard solutions in acetonitrile in a ratio of 35:65 with different concentrations: 0.025 mg/ml and 0.05 mg/ml were prepared, a calibration curve was created with a flow rate of 1 ml/min, a thermostat temperature of 40 0 °C , and an injection sample volume of 10 µl. Based on the standard samples, the corresponding chromatograms were obtained on a YSSX (LC 2030 C3D Plus Shimadzu , Japan) device for 2.5 min. gallic acid, 3.6 min. rutin, and 16 min. quercetin .

When performing the analysis of apigenin and kaempferol, a chromatogram was obtained in gradient mode for 12 min at a flow rate of 0.75 ml/min based on the above device parameters (Table 30.1) [193; p. 12-19].

Table 3.1.

Gradient mode of apigenin and kaempferol analysis

Time	C phase % 0.5% solution of acetic acid in water	Phase B % Acetonitrile
1	60	40
3	70	30
6	55	45
10	80	20
12	Stop	

### 3.4 -§. Determination of antioxidant activities of mixtures prepared from saffron crocus and flax seeds

Antioxidant activity is determined through phytochemical studies of the studied preparations and evaluated using several methods.

The antioxidant activity of the drugs is similar to that of adrenaline. *in vitro* It is determined by the inhibition of the autooxidation reaction and the prevention of the formation of free oxygen species under these conditions. The method is based on the inhibition of the auto-oxidation reaction of adrenaline, the use of drugs The amount of adrenaline produced and autoxidized *in vitro* over time is expressed as a percentage (%).

We determined the sample with the highest antioxidant activity among the samples prepared by mixing saffron florets and flax seeds in different mass ratios, designated ZF-1 (saffron), ZF-2 (saffron, flax – 3:1), ZF-3 (saffron, flax – 1:1) and ZF-4 (saffron, flax – 1:3), using the *in vitro adrenaline autooxidation method*.

To perform the work, 2.0 ml of 0.2 M sodium carbonate ( $\text{Na}_2\text{CO}_3$ - $\text{NaHCO}_3$ ) buffer with pH=10.65, 56  $\mu\text{l}$  of 0.18% adrenaline (epinephrine) hydrochloride solution are taken, 30  $\mu\text{l}$  of antioxidant sample is added and, after rapid mixing, it is examined in a 10 mm cuvette at a wavelength of 347 nm for 30 seconds to 10 minutes in a Cary 60 UV-Vis Agilet Technologies spectrophotometer. The amount of the substance under study (concentration of the extract in 1 ml is 1 mg) is standard As a control sample, 0.2 M 2.0 ml buffer, 0.18% 56  $\mu\text{l}$  (5.46 mM) adrenaline is used.

Antioxidant activity is expressed as a percentage of the inhibition of adrenaline autooxidation and is calculated by the following formula.

$$AA\% = \frac{D_1 - D_2 \times 100}{D_1} (3.2).$$

In this:

$D_1$  – to the buffer optical density of the added adrenaline hydrochloride solution;

$D_2$  – optical density of the extract under study and adrenaline hydrochloride added to the buffer [194; pp. 117-121].

### **§ 3.5. Determination of antiradical activity of the medicinal food supplements “ASQAND” and “ASUK”**

In this study, we used a spectrophotometric method to measure the kinetics of the reduction of the stable radical 2,2-diphenyl-1-picrylhydrazyl (DFPG) molecules by antioxidants to assess ARF. The method is based on the interaction of antioxidants with the stable chromogenic radical 2,2-diphenyl-1-picrylhydrazyl (DFPG).

A standard solution of DFPG ( $5 \times 10^{-4}$  M) in ethanol acidified with acetic acid was diluted with ethanol in a ratio of 1:10 to obtain a working solution. The resulting solution should have an optical density of not more than 0.9 at 517 nm. 50  $\mu$ l of extracts from the studied plants were added to 5 ml of DFPG working solution, mixed, and the kinetics of the decrease in optical density of the solution was recorded at a wavelength of 517 nm for 30 minutes. The DFPG working solution was used as a control sample. The antiradical activity was determined according to the following formula (formula 3.3) [195; pp. 2058-2070].

Since the “ASUK” medicinal food supplement consists of oils and is insoluble in water and ethanol, its antiradical activity was carried out in ethyl acetate solutions [172; pp. 17-27].

A working solution of DFPG in ethyl acetate with a concentration of 0.1 mM was used for the experiment. Solutions of the food additive “ASUK” in ethyl acetate with concentrations of 25  $\mu$ l/ml, 50  $\mu$ l/ml, 75  $\mu$ l/ml and 100  $\mu$ l/ml were taken as test samples, 100  $\mu$ l of which were measured, 2.9 ml of DFPG solution were added, mixed and the kinetics of the decrease in optical density of the solution was recorded for 30 minutes at a wavelength of 517 nm.

$$\text{Inhibirlash}\% = \frac{A_{\text{kontr}} - A_x}{A_{\text{kontr}}} \times 100\% \quad (3.3).$$

In this:

$A_x$  – optical density of the test solution,

$A_{\text{counter}}$  - the optical density of the test sample.

### **§ 3.6. Determining the effect of the medicinal food supplement “ASQAND” on the body’s oxygen consumption in conditions of hypoxia**

To prepare a solution of the “ASQAND” medicinal food supplement, 10 ml of ethanol was added to 10 ml of glycerin, and then 80 mg of the “ASQAND” medicinal food supplement was added to it. Male white rats weighing 180-200 g were selected for the experiment.

The animals were divided into 6 groups: the first was a control group, the second received 16, the third - 32, the fourth - 48, the fifth - 64, the sixth - 80 mg per kg of body weight. Samples were injected into the abdominal cavity. The oxygen exchange of K was determined by the polarographic method. For this, the animals were placed in hermetic chambers. A Clark electrode was placed in the chamber, which is sensitive to the oxygen content in the environment [ 178; 709-716-b ].

### **3.7-§. Study of the effect of the medicinal food supplement “ASQAND” on the process of lipid peroxidation**

The isolation of LPO products was carried out in the presence of thiobarbituric acid (TBK). The reaction was stopped by adding 0.220 ml of 70% trichloroacetic acid to the IM . After this step, the mitochondrial suspension was centrifuged at 4000 rpm for 15 minutes. Then 2 ml of the supernatant was removed and 1 ml of 75% thiobarbituric acid (TBK) was added. 2 ml of H<sub>2</sub>O and 1 ml of TBK were added to the control tube. The mixture was incubated in a water bath for 30 minutes. After cooling, the change in optical density at a wavelength of 540 nm was determined. To determine the amount of malondialdehyde (MDA) , the molar extinction coefficient ( $\epsilon=1.56 \times 10^5 \text{ M}^{-1} \text{ cm}^{-1}$ ) was used in the formula: nmol MDA/mg protein= $D/1.56 \times 30$ . Also, to study the LPO process in the mitochondrial

membrane, the Fe<sup>2+</sup>/ascorbate system was used. Under the influence of this system, the mitochondrial membrane lost its barrier function, as a result of which the organelle volume increased and the mitochondria swelled. This volume change was determined photometrically. IM: KCl - 125 mM, tris-HCl - 10 mM, pH 7.4; Concentrations: FeSO<sub>4</sub> - 10 μM, ascorbate - 600 μM; mitochondrial content 0.5 mg/ml [196; 165-180-p.].

### **3.8-§. Determination of the toxicity level of the medicinal food supplement “ASQAND”**

We conducted our studies on the determination of acute toxicity of the medicinal food supplement «ASQAND». The acute toxicity was determined using the Litchfield and Wilcoxon method in experimental groups of 6 male white laboratory mice with a body weight of 25±2.0 g.

All pharmacological studies were conducted on healthy, sexually mature mice kept in quarantine for 10-14 days. The studied “ASQAND” medicinal food supplement was administered into the mice’s mouths through a special probe at doses of 200, 400, 800 and 1000 mg/kg. During the experiment, the general condition of the animals of the experimental and control groups, possible tremors and deaths as an indicator of the functional state, were monitored every hour on the first day in laboratory conditions. Over the next 2 weeks, daily examinations were conducted in vivarium conditions in all groups for the general condition, activity, fur coat, skin condition, respiratory rate and depth, urine output rate, body weight change and other indicators.

All experimental animals were maintained on the same standard diet, with unlimited access to food and water. [197; pp. 13-17].

At the end of the experiment, the median lethal dose (LD<sub>50</sub>) and toxicity class of the “ASQAND” medicinal food supplement were determined.

Statistical calculation book of the obtained results Excel was carried out based on the program.

### **3.9-§. Determining the anti-diabetic effect of the medicinal food supplement “ASQAND”**

Experimental design. For our experiments, humane treatment of experimental animals was carried out in accordance with the Declaration of Helsinki (World Medical Association, Edinburgh, 2000) and the “Guidelines for the Use of Experimental Animals”. The alloxan diabetes (AD) model was chosen for our experiments. The studies were studied in the following groups.

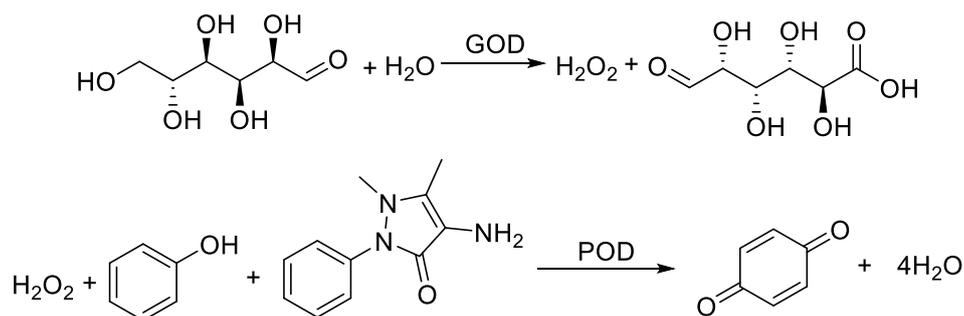
1. Intact group
2. Diabetes group
3. Diabetes group+diabeton
4. Diabetes+ “ASQAND” medical food supplement

Induction of diabetes model. The experimental model of diabetes mellitus is a method that allows studying the mechanism of the disease and developing the most convenient and effective methods of treatment with antioxidant drugs. During the study period, a total of 16 laboratory white rats were used, the weight and glucose content of the animals were measured and divided into groups. The day before the induction of the diabetes model, the animals were starved and given a 4% ascorbic acid (vitamin C) solution, the main reason for which is to prevent the death of animals in conditions of early hyperglycemia. Alloxan was administered to the animals. Low-sensitivity (chronic) alloxan diabetes method 8 mg/100 g alloxan monohydrate (Lachema, Czech Republic) dissolved in 0.9% NaCl solution and 0.5 ml was administered intraperitoneally to each animal for 8 days.

To prevent the animals from dying from hyperglycemia, the QD model was given honey water and boiled bovine brain. The blood of laboratory animals was used as the object of the study [198; p. 240].

The experimental animal model groups with diabetes were given the “ASQAND” medical food supplement and the drug Diabeton at a dose of 30 µg/ml.

Glucose determination. Glucose was determined using the Enzymatic-colorimetric test. GOD-POD (Cypress Diagnostics, Belgium) kit. The enzyme glucose oxidase oxidizes D-glucose to glucuronic acid with the formation of H<sub>2</sub>O<sub>2</sub>. Then, under the influence of peroxidase, it reacts with 4-aminoantipyrine and phenol to form a colored compound. The color intensity depends on the glucose concentration in the sample being tested and is measured photometrically at a wavelength of 505 nm.



We calculated the glucose concentration according to the following formula:

$$C_{Glyukoza} = \frac{Abs_{na'muna}}{Abs} \times 100 \times 0,0555 \text{ mmol/l} (3.4).$$

Determination of glycated hemoglobin. Under the influence of thiobarbituric acid, erythrocyte hemolysate undergoes acid hydrolysis to form 5-oxymethylfurfural. This allows the determination of glycated hemoglobin (%HbA<sub>1c</sub>) in erythrocytes. Glycated hemoglobin is calculated relative to 1% hemoglobin [199; pp. 281-283].

$$X = \frac{Ekstintsiya \text{ eritmasi}}{0,029} = \%HbA_{1c} (3.5).$$

Determination of hemoglobin content. Hemoglobin was determined using the “EKOlab” test kit (Russia). Blood hemoglobin is oxidized to methemoglobin by reacting with red blood cell salt, forming acetocyanhydrin hemoglobin cyanide, and the color intensity is proportional to hemoglobin and is measured photometrically at a wavelength of 540 nm.

Hemoglobin concentration was calculated according to the following formula:

$$C_{\text{Gemoglobin}}\left(\frac{g}{l}\right) = \frac{E_{\text{tajriba}}}{E_{\text{kalibrator}}} \times C_{\text{kalibrator}}(145 \text{ g/l}) \quad (3.6).$$

Glycogen determination. In the method used for the quantitative determination of glycogen in muscle and liver tissues, glycogen is precipitated using desmolized alcohol in an alkaline medium. The essence of the method is that muscle and liver tissue are desmolized with 30% KOH. The glycogen/glucose formed as a result of hydrolysis reacts with anthrone in the presence of H<sub>2</sub>SO<sub>4</sub> to give a blue mixture. It is calculated using the following formula:

$$C_{\text{Glikogen}} (\text{mg}\%) = \frac{0,05 \cdot E_{\text{nazorat}} \cdot A \cdot B}{E_{\text{ks}} \cdot 1,11 \cdot 1000} \quad (3.7).$$

In this case, the amount of glucose in mg of the standard solution is 0.05.

To convert 1000 to grams,

A—the amount of water in glycogen,

B—tissue theft,

Relative extinction factor of glycogen from 1,11—glucose,

E—control extinction.

Standard extinction of Ex—glucose [200; pp. 19-31].

### **3.10-§. Determining the anti-inflammatory effect of the medicinal food supplement “ASUK”**

**Carrageenan tumor model.** The experiments were carried out in a model of acute exudative inflammation induced by subplantar injection of carrageenan, a classical phlogogen. The experiment was performed in male and female rats with a body weight of  $160 \pm 15$  g. The food additive “ASUK” and glycerin were administered by gavage in doses of 0.25 ml and 0.5 ml, and 1 hour later, a 1% solution of carrageenan was injected into the apaneurosis of the hind paw of the rats in a volume of 0.1 ml. The initial volumes of the hind paws of the animals in the experimental and control groups were measured before carrageenan injection. The anti-inflammatory effect of the drugs was recorded at 1 -, 2 -, 3 -, 4 -, 5 - hours

and 24 - hours after the induction of inflammation. The size of the tumors was estimated based on the difference between the volumes of the non-inflamed and inflamed hind paws. The AEF of the drugs was determined in percentage by the difference in the reduction of tumors in the hind paws of experimental animals compared to the control [190; p. 944].

Antiexudative activity is calculated by the following formula:

$$AEF\% = \frac{\Delta V_{taj} - \Delta V_n}{\Delta V_n} \times 100\% (3.8).$$

In this AEF - antiexudative activity, in percent ;

$\Delta V_n$  – hind paw volume of the control group;

$\Delta V_{taj}$  - hind paw volume of the experimental group.

**Cotton granuloma model.** The «cotton granuloma» method was used to evaluate the antiproliferative and antiexudative effects of the studied drugs . The experiments were conducted on 30 white rats weighing  $160 \pm 15$  g . Nembutal was injected intraperitoneally at a dose of 50 mg/kg, the hair was shaved off in the dorsal shoulder area of the anesthetized rats, and the skin was cut with scissors under aseptic conditions, and the skin and subcutaneous tissue were opened 1-2 cm in length. Then, a pre-sterilized 10 mg cotton ball was inserted subcutaneously through the incision with tweezers, and then the skin incision was closed with a suture. The study food supplement “ASUK” and glycerin were administered orally for 7 days in doses of 0.25 and 0.5 ml, and the control group received corresponding volumes of distilled water. On the 8th day of the experiment, the implanted cotton ball was removed together with the granulation tissue formed around it, weighed, and dried at  $55-60^\circ \text{C}$  until its weight stabilized. The mass of the exudate (EM) was calculated based on the difference between the wet cotton ball and the dried cotton ball, and the mass of the formed granulation scar tissue (GM) was calculated based on the difference between the dried cotton ball and the mass of the cotton ball measured before implantation (10 mg) [191;].

The antiproliferative inflammation effect of the drugs was evaluated in percentage terms based on the suppression of the exudation process (EB) of these drugs:

$$EB = \frac{EM_{naz} - EM_{taj}}{EM_{naz}} \times 100\% (3.9).$$

and suppression of proliferation (PB, in percent):

$$PB = \frac{GM_{naz} - GM_{taj}}{GM_{naz}} \times 100\% (3.10).$$

In this case,  $EM_{Taj}$ . exudate mass in experimental groups;

$EM_{naz}$ . exudate mass in control groups;

Dry granuloma mass in  $GM_{taj}$ . experimental groups;

Dry granuloma mass in  $GM$  control groups.

The quantities in the formula:  $EM_{taj}$ ,  $EM_{naz}$ ,  $GM_{taj}$ ,  $GM_{naz}$ . are measured in mg units.

### Conclusions on Chapter III

By using methods to determine the chemical composition and biological activity of olive oil and saffron crocus, which were the objects of the study:

1. The content of macro and microbiological elements in saffron florets was determined by optical emission spectrometry;

$\beta$  -carotene in saffron crocuses was examined spectrophotometrically. Experiment The optimal conditions for determining the amount of  $\beta$  -carotene using this method were studied;

3. When analyzing the content of phenolic and flavonoid compounds such as gallic acid, rutin, apigenin, and kaempferol in saffron crocuses using the YSSX method, it was determined that these compounds were present in saffron crocuses;

4. The antioxidant activity of samples prepared from saffron flower buds was studied using the adrenaline autooxidation method. The antioxidant activity of samples prepared from olive oil was also tested using the same method, but DMSO was used as a solvent, taking into account the insolubility of oils in water;

5. The stable radical 2,2-diphenyl-1-picrylhydrazyl (DFPG) method was chosen to quantitatively assess the antiradical activity of the obtained food additives. Ethyl acetate was used as a solvent to determine the antiradical activity of the food additive “ASUK”;

the medicinal food supplement “ASQAND” in solution, based on saffron crocuses, on oxygen consumption under hypoxic conditions was studied; the effect

medicinal food supplement “ASQAND” based on saffron crocuses on the process of lipid peroxidation was carried out using the iron-ascorbate system;

medicinal food supplement “ASQAND” based on saffron crocus was tested using the Litchfield and Wilcoxon method;

medicinal food supplement “ASQAND” based on saffron crocus were evaluated in vivo;

10. The anti-inflammatory activity of the olive oil-based medicinal food supplement “ASUK” was tested in vivo using the “Carrageenan Swelling” and “Cotton Granuloma” methods;

## **CHAPTER IV. PRODUCTION OF MEDICINAL FOOD ADDITIVES FROM OLIVE AND SAFFRON PLANTS AND CLASSIFICATION BASED ON THEIR CHEMICAL COMPOSITION**

### **§ 4.1. Preparation and industrial production of a medicinal food supplement called “ASQAND” based on saffron stigmas**

Research has shown that saffron has long been widely used as a natural product that is very useful in preventing and treating many diseases, such as diabetes, cancer, cardiovascular diseases, allergic diseases, and nervous disorders [30; pp. 426-432].

We prepared test samples from mixtures of saffron florets and flax seeds in different proportions and, in order to determine their biological properties, first determined their antioxidant activity *in vitro*. The mixture of saffron and flax in a 1:3 mass ratio showed the highest antioxidant activity.

In the next stage of our research, we conducted a series of *in vivo* experiments on a mixture of saffron crocus and flax seeds in a 1:3 mass ratio. In particular, we examined its antidiabetic activity. During the experiment, it was found that the sample has high antidiabetic activity.

We planned to prepare a medicinal food supplement based on a mixture of saffron crocuses and flax seeds in a 1:3 mass ratio and call it “ASQAND”.

For the industrial production of finished food additives from saffron crocus and flax seeds, plant-based raw material mixtures must meet a number of technical requirements, namely, the raw material mixture must comply with the requirements of the current state standard and technological instructions.

raw materials must comply with the amounts specified in Sanitary Requirements No. 0366-19 (San PIN) [201; p. 95].

Raw materials showing signs of spoilage are not allowed to be processed. Raw materials are stored in a dry, cool, well-ventilated room at a temperature not exceeding 20 °C and a relative humidity not exceeding 75%.

The raw materials are ground in a mill to the appropriate particle size in accordance with the requirements of DSt 1936 and sieved, and then the ground raw materials are sent for packaging in accordance with DSt 24027.1.

The finished herbal tea is packaged in soft cellulose packaging approved by the Ministry of Health of the Republic of Uzbekistan for use in food and food products. The weight is determined on SW-2 scales with a resolution of 0.001 g according to DSt 29329.

Phytoteas are packaged in bags made of polymer and combined materials according to DSt 12302, polyethylene films according to DSt 10354, paper-based combined materials according to DSt 7247, DSt 24370, bags and sachets intended for single-use preparation weighing up to 2 g [202; TY 304553567-03:2023].

Having studied the chemical composition of saffron crocuses, we began to produce a new food additive from them, based on the scientifically based results obtained. In this practice, drying, grinding and packaging of raw materials were carried out using DKX-II Multi Auto Oven, CSJ-100 and A-320 devices, respectively.

The cost of producing the food additive “ASQAND” was calculated. The table below shows the cost determined as a result of the calculation Table (4.1).

Table 4.1.

Information about the composition and cost of the food supplement “ASQAND”

Raw material products			Production costs			Total
Saffron	Flax	Green tea	Packages	Box and corrugated	Workforce vs.	
0.1 g	0.3 g	49.6 g	25 pieces	1 piece	1 piece per box	
Price (in soums)						
4500	40	1390	200	540	460	7130

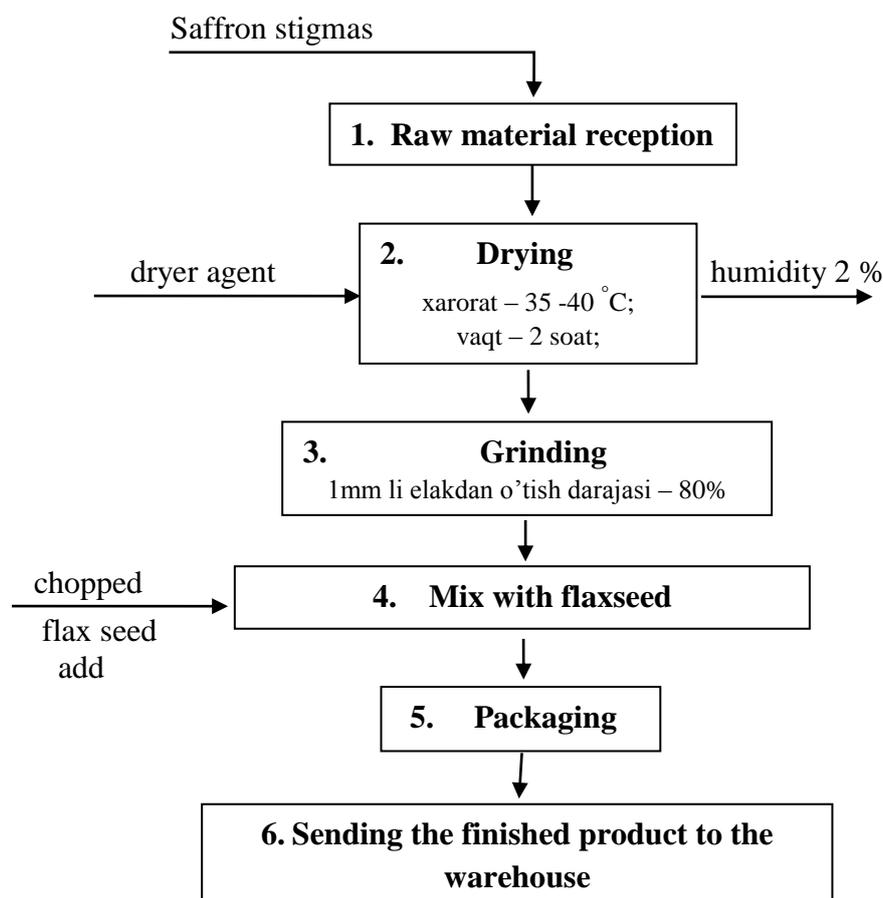


Figure 4.1. The main technological scheme for the production of the food additive «ASQAND».

1. Quality raw materials are selected; 2. Raw materials are dried in the DKX-II Multi Auto Oven; 3. Raw materials are ground in a CSJ-100 device; 4. Raw material components are mixed; 5. The product is packaged in 2-gram packets in an A-320 packaging device and packed in boxes; 6. Finished products are sent to the warehouse.

Technological instructions for the production of a new medicinal food supplement called “ASQAND” based on saffron crocuses (Appendix 1) have been developed, and a sanitary and epidemiological conclusion has been obtained from the Sanitary and Epidemiological Wellbeing and Public Health Service under the Ministry of Health of the Republic of Uzbekistan (Appendix 2). Today, serial production of the “ASQAND” food supplement is being launched at the “ZAYTUN MED GROUP” LLC enterprise operating in the Altinkol district of Andijan region.

## **§ 4.2. Preparation and industrial production of a medicinal food supplement called “ASUK” based on olive oil**

Olive oil has been widely used in folk medicine for various diseases, including inflammatory diseases. However, there is no information about the production of a food supplement consisting of a mixture of olive oil and flaxseed oil.

*in vitro* to evaluate their biological properties. The 3:1 mixture of olive and flaxseed oils showed the highest antioxidant activity.

the anti-inflammatory activity of a 3:1 mixture of olive and flaxseed oils *in vivo* using methods such as carrageenan edema and cotton granuloma. It was noted during the experiment that this sample had high anti-inflammatory activity.

Therefore, we set ourselves the goal of creating a food supplement consisting of a mixture of these two oils and determined the properties of their mixture in different proportions. Based on the results of our experiments, we developed a food supplement called “ASUK”, consisting of a 3:1 mixture of olive and linseed oils.

Since this product is oily in nature, its production requires studying the requirements for the production of oils.

Olive and linseed oils for product production must have the following valid regulatory documents:

### **Normative indicators;**

- DSt 26927-86 Raw materials and food products, methods for determining mercury

- DSt 26929-86 Preparation of samples of raw materials and food products. Mineralization for the determination of toxic elements

- DSt 26930-86 Raw materials and food products, methods for determining arsenic

- DSt 26932-86 Raw materials and food products, methods for determining lead

- DSt 26933-86 Raw materials and food products, methods for determining cadmium

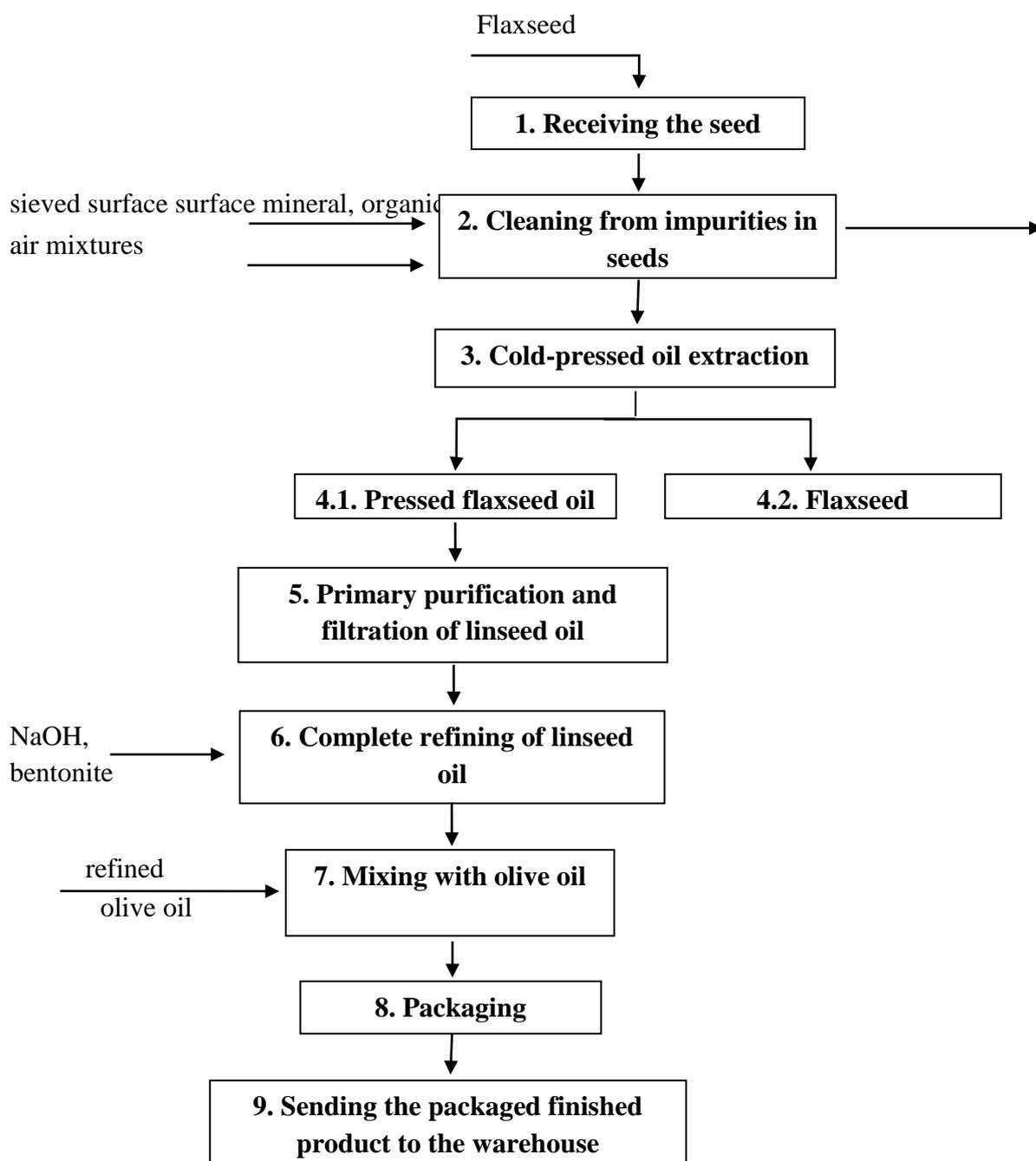
- DSt 30178-96 Raw materials and food products, atomic adsorption method for the determination of toxic elements

- DSt 11812-66 Methods for the determination of vegetable oils, moisture and volatile substances

Production to release By San PiN 0366 - 2019 installed out of order excess normally pesticides, toxic elements, nitrates , radionuclides and microbiological to indicators has happened raw materials not used [203; San.Pin.].

Production issued products packaging every one in the department offset printed label to be or from following the data itself inside received packaging in the material working issuer name, brand symbol, its legal and real address, phone, product name, composition, pure weight, work issued date (day, month, year), expiration date, 100 g product for nutritional and energy value about information, storage Terms and conditions, registration number is shown barcode, O'zDSt 5.8 suitable incoming compatibility symbol, this standard designation, product from Uzbekistan Republic from the territory outside sell for « In Uzbekistan “Working released” writing such as the data itself inside received template to be need [204; TY 304553567-02:2023].

The production of the “ASUK” food supplement includes the following stages: 1. High-quality flax seeds are selected; 2. Flax seeds are cleaned of various mineral and organic impurities; 3. Oil is obtained by cold pressing the seeds; 4.1. The oil obtained by pressing is separated from solid inclusions; 4.2. Solid inclusions can be sent for secondary processing or used as feed for livestock; 5. Flax oil undergoes primary purification by filtration; 6. Purified flax oil undergoes a complete refining process using sodium hydroxide and bentonite; 7. The resulting flax oil is mixed with olive oil; 8. The mixture of oils is poured into 50 ml bottles and placed in boxes; 9. Packaged finished products are sent to the warehouse.



The main technological scheme for the production of the food additive “ASUK”.

Table 4.2.

Results of sanitary and hygienic inspections of the biological food supplement «ASUK»

No .	Test parameters	Regulatory document	According to NTX (mg/kg)	Actual value (mg/kg)	Indicator compatibility
1	Zinc	DSt 26934-86	5.0	0.66	Fits
2	Cadmium	DSt 26933-86	0.05	0.00	Fits
3	Lead	DSt 26932-86	0.1	0.00	Fits
4	Copper	DSt 26931-86	0.5	0.028	Fits
5	Arsenic	DSt 26930-86	0.1	0.00	Fits
6	Mercury	DSt 26927-86	0.03	0.00	Fits
7	Iron	DSt 26928-86	5.0	0.73	Fits
8	Acidity number	DSt 21933-2012	0.4-0.5 mg	0.44 mg KOH/g	Fits

			KOH/g		
9	Peroxide number	DSt 26593-85	10 mmol active oxygen/kg	8.15 mmol active oxygen/kg	Fits

Based on the information presented in the table, it can be said that the “ASUK” medical food supplement fully meets all sanitary and hygienic requirements (Table 4.2.).

The cost of the food supplement “ASUK” has been calculated. The table below presents this information (Table 4.3.).

Table 4.3.

Information about the composition and cost of the food supplement «ASUK»

Raw material products		Production costs			Total
Olive oil	Flaxseed oil	Vial (50 ml)	Box, label and corrugated	Workforce vs.	
37.5 ml	12.5 ml	1 piece	1 piece	1 piece per box	
Price (in soums)					
4350	1850	500	540	460	7700

Currently, the relevant technological instructions (Appendix 3) have been developed for the olive-based medicinal food supplement “ASUK” and a sanitary-epidemiological conclusion has been obtained from the Sanitary - Epidemiological Wellbeing and Public Health Service under the Ministry of Health of the Republic of Uzbekistan (Appendix 4). Serial production of the “ASUK” food supplement is being launched at the “ZAYTUN MED GROUP” LLC enterprise operating in the Altinkol district of Andijan region.

#### **4.3 -§. Classification of medicinal food supplements “ASQAND” and “ASUK” based on saffron crocus and olive oil according to their chemical composition and development of a commodity code according to the Nomenclature of Foreign Economic Activity Goods**

All types of goods produced in Uzbekistan have been subject to international declaration since January 1, 1994 [23].

Based on the Harmonized System (HS), all types of goods are classified according to 6 rules that are used in practice and are assigned international code numbers. According to rules 1-5, goods are classified up to 4-digit numbers depending on the position of the goods. HS defines the basic rules for classifying goods. These rules require a uniform interpretation in HS. In essence, TIF operates on the basis of HS. In classifying goods based on the nomenclature of goods for foreign economic activity, their main indicators are determined: characteristics of materials or components, volume, quality, quantity, weight, value, and potential for foreign trade [205; 290-b].

Any manufactured goods are classified according to their chemical composition and international commodity code numbers are assigned to these goods according to the Commodity Nomenclature of Foreign Economic Activity. Currently, goods manufactured in Uzbekistan are assigned international commodity code numbers in accordance with the TIF TN, approved by the Decree of the President of the Republic of Uzbekistan No. PF-460 dated December 28, 2022 and entered into force on January 1, 2023. This latest version of the TIF TN includes 21 sections and 97 groups. In addition to the 97 groups, 3 groups (77, 98, 99) are reserved. The 21 allocated sections are divided into: 1252 positions, 5367 subpositions and 11293 subsubpositions. The 2017 version of the Customs Tariff of the Republic of Uzbekistan includes additions and changes to 233 commodity headings. Of these, a total of 36 commodity headings were added, 79 commodity headings were removed, and additions were made to 3 commodity groups. 205 subheadings were added and 43 subheadings were removed, since the goods included in the 43 removed subheadings are currently not in demand in the foreign market [206].

“Obtaining and classifying medicinal food additives based on olive and saffron plants” conducted in the “Commodity Chemistry” scientific laboratory operating at the Department of Chemistry of Andijan State University, the chemical composition of olive and saffron plants was studied. Taking into account the beneficial and medicinal properties of olive and saffron for the human body,

“ASQAND” and “ASUK” food additives were prepared from them and recommended for consumption by patients.

When developing commodity codes for food additives “ASQAND” and “ASUK” made from saffron, olive oil, and flax seeds and oil, if we look at the TIF TN, saffron is included in section II, which includes “Products of plant origin”, item 09. group, i.e. coffee, tea, mate or Paraguay tea and spices, 0910 – ginger, saffron, turmeric (curcuma), mountain jambil or chabres, bay leaf, curry and other spices, 091020 – saffron, the commodity codes 0910201000 and 0910209000 are assigned to unground and uncrushed as well as crushed or crushed products, respectively [206; p. 95].

Flaxseed is also classified in Section II of the TIF TN, 12 – Oilseeds and fruits; other seeds, fruits and grains; medicinal plants and plants for technical purposes; straw and fodder products, in the group 120400 – flaxseed, whether or not ground, under commodity codes 120400100, 1204001001 and 1204001009 [206; p. 106].

linseed oil and its fractions in Section III, 1515 – other fixed fats and oils and their fractions, whether or not refined or refined without changing their chemical composition [206; p. 119].

For olive oil, Section III – Fats and oils of animal, vegetable or microbiological origin and their cleavage products; prepared edible fats; waxes of animal and vegetable origin; 15 – Fats and oils of animal, vegetable or microbiological origin and their cleavage products; prepared edible fats; waxes of animal and vegetable origin, heading 1509 – Olive oil and its fractions, whether or not refined, but not chemically modified, - extra virgin olive oil; - virgin olive oil; - other virgin olive oils are designated by the commodity codes 1509200000, 1509300000 and 1509400000 respectively [206; [p. 116].

Since the food additives “ASQAND” and “ASUK” are composite products consisting of mixtures of various plants, it is not possible to represent them with the above commodity code numbers.

Taking this into account, we classified the food supplement “ASQAND” under subheading 121230 – “Food supplements made from medicinal plants or their parts” of the Nomenclature of Goods in Foreign Economic Activity, and recommended the commodity code number 1212 301503 for “Natural food supplements made from medicinal plants or their parts containing crocetin, crocin, beta-carotene, safranal” (Table 4.4.).

Table 4.4.

Recommended product code number for the medicinal food supplement “ASQAND” according to TIF TN

<b>TIF TN Code</b>	<b>Naming of positions</b>
121230	- doctor from plants, or some of them from parts prepared food – food additions ;
121230150	- others ;
1212301503	- “ASQAND” food supplement containing saffron crocuses and flax seeds;

We classified the food supplement “ASUK” under heading 2106 - Food products not elsewhere specified or included; 210690 - Others; and recommended the commodity code number 2106 90 980 6 for “natural food supplements containing oleic acid, palmitic acid, linoleic acid and their esters, tyrosol and hydroxytyrosol, prepared from medicinal plants or their parts” (Table 4.5.).

Table 4.5.

Recommended commodity code number for the medicinal food supplement “ASUK” according to TIF TN

<b>TIF TN code</b>	<b>Naming of positions</b>
2106	- food products not elsewhere specified or included;
2106 90	- others ;
210690980	- others ;
210690980 6	- “ASUK” food supplement containing olive and linseed oils;

The commodity code number 2106909806 proposed by us for the food additive «ASUK» was accepted by the Customs Committee of the Republic of Uzbekistan and a corresponding certificate was issued (certificate of the State

Customs Committee of the Republic of Uzbekistan No. 17/05-24-1187 dated June 20, 2024).

#### **Conclusions on Chapter IV.**

the practical use of the biological activity and healing properties of olive oil and saffron crocuses, which were taken as the object of research, and their classification according to their chemical composition:

1. For the industrial production of food additives based on olives and saffron, raw materials were selected that were, first of all, environmentally friendly, chemical composition, and organoleptic properties that met the requirements of the state standard.

2. Technical safety in the production process of food additives based on olives and saffron, sanitary and hygienic requirements for technological devices, and compliance with state standards for chemical and biochemical analysis of the manufactured product were ensured.

3. Medicinal food supplements “ASQAND” and “ASUK” based on olives and saffron were created, and the production of these products was launched at the “ZAYTUN MED GROUP” LLC enterprise operating in the Altinkol district of Andijan region.

## CONCLUSION

As a result of the research carried out within the framework of the dissertation work on the topic “Obtaining and classifying medicinal food additives based on olive and saffron plants”, we came to the following general conclusions:

$\beta$  – carotene in saffron crocuses grown in the Surkhandarya region of our republic was examined.

2. The “ASUK” medicinal food supplement was created based on olive oil, and the “ASQAND” medicinal food supplement was created based on saffron crocus.

3. The results of quantitative evaluation of the antiradical activity of the obtained food additives relative to the stabilizing radical 2,2-diphenyl-1-picrylhydrazyl (DFPG) showed that they have high antiradical properties.

4. The anti-inflammatory activity of the olive oil-based food supplement “ASUK” was tested *in vivo* using the “Carrageenan Swelling” method and the antioxidant properties of the “Cotton Granuloma” method, and it was proven that these properties are higher than those of some synthetic agents.

5. The effect of the saffron-based food supplement “ASQAND” on glycogen in liver and muscle tissues and on the amount of glycosylated hemoglobin and free hemoglobin in the blood was evaluated *in vivo*.

6. As a result of studying the effect of the “ASQAND” food supplement on blood sugar levels in laboratory rats under *in vivo* conditions, it was proven that its hypoglycemic properties are more effective than the synthetic drug “Diabeton”.

7. The food additive “ASQAND” is classified under subheading 121230 - “Food additives prepared from medicinal plants or their individual parts” of the Nomenclature of Goods in Foreign Economic Activity, and is included in the category “Natural food additives prepared from medicinal plants or their individual parts containing crocetin, crocin, beta-carotene, safranal, etc. For “Additives” - the commodity code number 1212 301503 was recommended.

8. The food additive “ASUK” is classified under heading 2106 - food products not elsewhere specified or included; heading 210690 - other; classified by

supposition, and the commodity code number 2106 90 980 6 was recommended for “Natural food additives prepared from medicinal plants or their parts containing oleic acid, palmitic acid, linoleic acid and their esters, tyrosol and hydroxytyrosol”.

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# APPENDICES

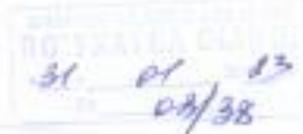
Appendix 1.

<b>«KELISHILDI»</b>	<b>«TASDIQLAYMAN»</b>
O'zbekiston Respublikasi Sog'liqni Saqlash Vazirligi Sanitariya-epidemiologik osoyishtalik va jamoat salomatligi xizmati Andijon viloyat shqarmasi boshlig'i	«ZAYTUN MED GROUP» Mas'uliyati cheklangan jamiyati Andijon viloyati Ditinko'l tumani
 D.A. NABIYEV	 B. MAKSUDOV
<u>31. yanvar</u> 2023 yil	<u>31. yanvar</u> 2023 yil

**QO'SHINCHALI CHOY ISHLAB CHIQARISH UCHUN  
TEKNOLOGIK YO'RIQNOMA**

O'zDSt 3466:2020 asosida  
TY 304553567 - 03:2023

O'zDSt 3466:2020  
asosida ishlab chiqarildi.  
  
A. Abduraxapov  
31. yanvar 2023 yil





**ЎЗБЕКИСТОН RESPUBLIKASI SOĞLIQNI SAQLASH VAZIRLIGI**

*SEOVAJSQ Andijon viloyat boshqarmasi Jalaquduq tuman bo'limi*  
(sanitariya-epidemiologik xulosasi berish muassasasi)

**O'ZAK SL 0312 17.07.2023**  
(sanitariya-epidemiologik xulosasi berish muassasasi)

**№ 386123**

**САНИТАРИЯ-ЭПИДЕМИОЛОГИК ХУЛОСА**

20 23 йил 7 avgust дан 20 26 йил 7 avgust гача ҳақиқий ҳисобланади.

Ушбу хулоса билан: "ZAYTUN MED GROUP" MCHJ (ишлаб чиқарувчи, ишлаб чиқариш объектлари, ишлаб чиқарувчи)  
ТҲ 304553567-03/2023.  
СанҚМ 0366-19 р.р 6,9

(ишловчи, маддий маҳсулотларни асосий ҳисоб қилиш ва ишлаб чиқариш)

Ишлаб чиқарилган (олиб келинган) маҳсулот: Qo'shimchali chuylar - ko'k choy fitochoy Alinab, ko'k choy fitochoy As Nabali, ko'k choy fitochoy Asqand 50,100 gramdan polimer va qarton idishlarda. (seriyali ishlab chiqarish uchun).  
San.kimyoviy tekshirishlar (og'ir metal tuzlari, pestitsidlar, mikotoksinlar) bo'yicha SanQM 0366-19 talabiga javob beradi. San.gig. laboratoriya bayonnomasi № 17-19 3 avgust 2023 yil va № 468 2 avgust 2023 yil. Mikrobiologik tekshirishlar (mog'or) bo'yicha SanQM 0366-19 talabiga javob beradi San.bak. laboratoriya bayonnomasi № 17/11-19/13 7 avgust 2023 yil. Radiologiya laboratoriya bayonnomasi № 233 2 avgust 2023 yil. MCHJ "ZAYTUN MED GROUP" MCHJ Sanitariya qonida va meъerlari talablariga javob beradi. SanQM 0366-19 talabiga javob beradi.

Хулоса олувчи: "ZAYTUN MED GROUP" MCHJ  
Andijon viloyat Oltiko'1 tuman Cho'ntak MFY. Korhona manzili: Andijon viloyat Andijon tuman Yangi-Yul MFY

Қўлланиладиган, ишлатиладиган соҳа: Oziq ovqat maqsadida.

Ишлатиш, ташин, сақлаш ва хавфсизлигига оид шарт-шаронглар: Sanitariya gigiena talablariga rioya qilgan holda.

Махсулотнинг санитария-эпидемиологик хулоса берилган муассаса мухри: epidemiologic hutosa muxsasi xulosa berilgan muassasa muxri xaqiqiy xisoblanadi.

  
A. Xolmatov  
(sanitariya-epidemiologik xulosasi berish muassasasi vakili, shifosi)

23 avgust  
20 23 йил 7 avgust

«KELISHILDI»



O'zbekiston Respublikasi  
Sog'liqni Saqlash Vazirligi  
Sanitariya-epidemiologik osoyishtalik  
va jamoat salomatligi xizmati  
Andijon viloyat  
boshqarmasi boshlig'i

*A. N. Ikramov*  
A. N. IKRAMOV  
«19» oktabr 2023 yil

«TASDIQLAYMAN»



«ZAYTUN MED GROUP»  
Mas'uliyati cheklangan jamiyati  
Andijon viloyati  
Oltinchi tumani

*B. Maqsudov*  
B. MAQSUDOV  
«18» oktabr 2023 yil

TURLI XIL O'SIMLIK MOYLARI ISHLAB CHIQARISH UCHUN  
TEXNOLOGIK YO'RIQNOMA

Maxsus texnik reglament  
MTR 724-023:2020 asosida

TY 304553567-02:2023

MTR 724-023:2020

Asosida ishlab chiqarildi.

*A. Abduraxapov*  
A. Abduraxapov  
«18» oktabr 2023 yil





**ЎЗБЕКИСТОН RESPUBLIKASI SOĞLIQNI SAQLASH VAZIRLIGI**  
**SEO va JSQ Andijon viloyatining Jalaquduq tuman bo'limi**  
**Akkreditatsiya guvohnomasi O'ZAK.SI. 0312**  
(akkreditatsiya olib olingan xizmatlarni berish maqsadida berilgan)

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(akkreditatsiya subektlarining o'zaro ishi va sharti)

**№ 386142**

**САНИТАРИЯ-ЭПИДЕМИОЛОГИК ХУЛОСА**

23 30 oktyabr 20\_\_ йил \* \* \* \* \* дан 26 30 oktyabr 20\_\_ йил \* \* \* \* \* гача ҳақиқий ҳисобланади.

Ушбу хулоса билини: **"ZAYTUN MED GROUP" MCHJ tomonidan ishlab chiqarilgan.**  
(ishlab chiqarish, ishlab chiqarish, ishlab chiqarish, ishlab chiqarish)

**TU 304553567-02-2023. San QM 0366-19 p.p. 7.1 UzTR 724-023-2020**

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(nizom, maqsadli maqsadlar va shartlar bilan bog'liq xizmatlar)

Ишлаб чиқарилган (олиб келинган) маҳсулот: **~~O'simlik moylari~~ : ASUK (ACYK) zig'ir moyi 25 % zaytun moyi 75 % aralashmasi. At tabib (Am tabib ) xantal moyi 70 % , oshqovoq moyi 30 % aralashmasi 25 ,50 ,100 ml shisha va pet idishlarga qadoqlangan.**

**/Seriya ishlab chiqarish uchun /**

**San. Kimyoviy ,radiologik, benzopiren laboratoriya tekshiruvlari bo'yicha San QM 0366-19. UzTR 724-023-2020 talabiga javob beradi. San.gig. laboratoriya tekshiruvlari bayonnomasi № 95-96 25-oktyabr 2023 yil. Benzopiren bo'yicha laboratoriya tekshiruvlari bayonnomasi № 77-962 30 oktyabr 2023 yil. Radiologiya laboratoriya tekshiruvlari bayonnomasi № 32-33 28-oktyabr 2023 yil**

Санитария қўяда ва меъралари талабларига **ЖАВОБ БERAДИ**  
**"ZAYTUN MED GROUP" MCHJ**

Ху.**Q'zbekiston Respublikasi Andijon viloyat Oltinko'l tuman Cho'ntak MFY .Sex manzili : Andijon tuman Poloson MFY.**  
(shart shartlar bilan bog'liq ishlab chiqarishni taqabildir)

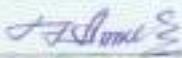
Қўлланиладиган, ишлатиладиган соҳа: **Oziq-ovqat maqsadida.**

Ишлатиш, ташвиш, сақлаш ва хавфсизлигига оид шарт-шароитлар **Sanitariya gigiena qoidalariga rioya qilgan holda.**

**Sanitariya -epidemiologik hulosa nuxsasi hulosa berilgan**

**Maqsadli maqsadli bo'lsa haqiqiy hisoblanadi.**

**A.Xolmatov**



(sanitariya-epidemiologik xulosaning berilish nuqtasi) 23 30 oktyabr 20\_\_ йил \* \* \* \* \*

20\_\_ йил \* \* \* \* \*

IJRO.GOV.UZ тизими орқали ЭРИ билан тасдиқланган, Ҳужжат коди: XR83872468



**O'ZBEKISTON RESPUBLIKASI**  
**SOG'LIQNI SAQLASH VAZIRLIGI HUZURIDAGI**  
**SANITARIYA-EPIDEMIOLOGIK OSOYISHTALIK**  
**VA JAMOAT SALOMATLIGI QO'MITASI**  
 SANITARY-EPIDEMIOLOGICAL WELFARE AND PUBLIC HEALTH COMMITTEE  
 UNDER THE MINISTRY OF HEALTH OF THE REPUBLIC OF UZBEKISTAN

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2024 yil. "16" may

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**nomidagi "ANDIJON DAVLAT**  
**UMIVERSITETI" rektoriga**

Ўзбекистон Республикаси Санитария-эпидемиологик осойишталик ва жамоат саломатлиги қўмитаси 2024-йил 7-майдаги 39-01-528-сонли мурожаат хат билан танишиб чиқиб қуйидагиларни маълум қилади.

Мазкур хат билан тақдим этилган **“ASUK” ва “ASQAND”** маҳсулотлари Ўзбекистон Республикаси Соғлиқни Сақлаш Вазирлиги ҳузуридаги Фармацевтика тармоғини ривожлантириш агентлиги, “Дори воситалари, тиббий буюмлар ва тиббий техника экспертизаси ва стандартизацияси давлат маркази” ДУКининг “Тиббиёт амалиётида қўлланилишига рухсат этилган дори воситалари, тиббий буюмлар ва тиббий техника ДАВЛАТ РЕЕСТРИ” рўйхатига шу номлар остида дори воситаси сифатида рўйхатдан ўтказилмаган.

Ушбу маҳсулотларнинг қўллаш йўриқномасида кўрсатилган маълумотлар кейинги босқичларда кўриб чиқилади.

Раиснинг биринчи ўринбосари



Н.Атабеков

Ижрочи: Ш.Арипов  
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**O‘ZBEKISTON RESPUBLIKASI IQTISODIYOT VA MOLIYA  
VAZIRLIGI HUZURIDAGI BOJXONA QO‘MITASINING  
MARKAZIY BOJXONA LABORATORIYASI**  
CENTRAL CUSTOMS LABORATORY OF THE CUSTOMS COMMITTEE UNDER  
THE MINISTRY OF ECONOMY AND FINANCE OF THE REPUBLIC OF UZBEKISTAN  
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2024 йил “ 20 ” июнь

№17/05-24-1187

**“ТАСДИҚЛАЙМАН”**

Ўзбекистон Республикаси Божхона  
қўмитасининг Марказий божхона  
лабораторияси бошлиғи ўринбосари,  
божхона хизмати капитани

Б.Даутов

“ 20 ” 2024 йил



**Убайдуллаев Комилжон Турсунбоевичнинг “Зайтун ва заъфарон  
ўсимлиги асосида шифобахш озик-овқат қўшилмалари олиш ва уларни  
синфлаш” мавзусидаги кимё фанлари бўйича фалсафа доктори (PhD)  
диссертацияси натижалари юзасидан**

**МАЪЛУМОТНОМА**

Андижон давлат университети Кимё кафедраси эркин тадқиқотчиси Убайдуллаев К.Т. томонидан к.ф.д., профессор Аскарлов И.Р. раҳбарлигида заъфарон асосида “ASQAND” ва “ASUK” озик – овқат қўшималари яратилган. Яратилган биологик фаол озик-овқат қўшимчаси учун техник йўриқнома ишлаб чиқилган, лаборатория текширувлари амалга оширилган, клиник синовлар ўтказилган ва амалиётга жорий қилинган.

Ўтказилган барча текширувларда озик-овқат қўшилмасининг ноҳўя таъсирлари кузатилмаган, клиник синовларда “ASQAND” ва “ASUK” озик – овқат қўшималари қондаги қанд миқдорини пасайтиришда ижобий натижалар кўрсатган. Ушбу маҳсулотга 2023 йилда Ўзбекистон Республикаси Соғлиқни Сақлаш Вазирлиги томонидан ТУ304553567-03:2023

рақамли “Техник йўриқнома”, №386123 сонли “Санитария-эпидемиология хулосаси” берилган. Андижон вилояти, Олтинкўл туманида фаолият олиб бораётган “ZAYTUN MED GROUP” МЧЖ томонидан “ASQAND” ва “ASUK” озиқ-овқат қўшималари серияли ишлаб чиқариш йўлга қўйилганлиги маълум қилинган.

Убайдуллаев К.Т. томонидан таркибида айрим доривор ўсимликлар сақловчи “ASQAND” ва “ASUK” озиқ – овқат қўшималарини кимёвий таркиби асосида синфлаб, уларга ташқи иқтисодий фаолиятдаги товар номенклатураси бўйича қуйидагича: “таркибида кроцетин, кроцин, бета-каротин, сафранал сақловчи доривор ўсимликлар ёки уларнинг айрим қисмларидан тайёрланган табиий озиқ-овқат қўшилмалари” учун – 2106 90 980 6 код рақамлари тавсия этилди.

Юқоридагиларни инобатга олган ҳолда, мазкур код рақам Товарларни таснифлаш ва кодлашнинг уйғунлаштирилган тизим асосида жорий этилган Ташқи иқтисодий фаолияти товар номенклатурасининг навбатдаги ахририли ишлаб чиқиш жараёнида кўриб чиқиш учун қабул қилинди.

**Марказий божхона лабораторияси ТИФ ТН  
бошқармаси Классификациялаш маркази  
бошлиғи**

**Р.Мурзаев**

**Марказий божхона лабораторияси ТИФ ТН  
бошқармаси ТИФ ТН юритиш бўлими  
катта инспектори**

**Э.Нурмонов**