

## Rhizomes of Ginger officinalis: scientific substantiation of application in modern medicine and approaches to the standardization of raw materials

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## The rhizomes of common ginger: the scientific rationale for the use in modern medicine and approaches to the standardization of crude herbal drugs

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### SUMMARY

An information-analytical study of scientific literature data on medicinal ginger was carried out. It has been established that the rhizomes of medicinal ginger (*Zingiber officinale* Roscoe, Zingiberaceae L.) are known and used all over the world. In Europe, it is used as a spice and food product, and is also used in medicine. The healing properties of ginger have long been known in the East, and the spectrum of its pharmacological activity and use in national medical systems is unusually wide. The chemical composition of ginger rhizomes has been well studied by now: biologically active substances that provide the main pharmacological effects are zingerone, gingerols and shogaols (gingerol). According to the data of preclinical and clinical studies conducted in many countries of the world, ginger rhizome has a positive effect on the state and functioning of almost all organs and systems of the human body, has anti-inflammatory, expectorant, hypoglycemic, antihypercholesterolemic, antiulcerogenic and hepatoprotective effects. It is effective in the complex therapy of such socially significant diseases as diabetes and diseases of the nervous system. Currently in Russia the quality of ginger rhizomes is regulated by GOST 29046-91 "Spices. Ginger. Technical conditions", a draft pharmacopoeial monograph was developed for ginger rhizomes, which was carried out taking into account modern requirements for quality standards of medicinal plant materials. antiulcerogenic and hepatoprotective action. It is effective in the complex therapy of such socially significant diseases as diabetes and diseases of the nervous system. Currently in Russia the quality of ginger rhizomes is regulated by GOST 29046-91 "Spices. Ginger. Technical conditions", a draft pharmacopoeial monograph was developed for ginger rhizomes, which was carried out taking into account modern requirements for quality standards of medicinal plant materials. antiulcerogenic and hepatoprotective action. It is effective in the complex therapy of such socially significant diseases as diabetes and diseases of the nervous system. Currently in Russia the quality of ginger rhizomes is regulated by GOST 29046-91 "Spices. Ginger. Technical conditions", a draft pharmacopoeial monograph was developed for ginger rhizomes, which was carried out taking into account modern requirements for quality standards of medicinal plant materials.

**Key words:** medicinal ginger, gingerols, shogaols, expectorant action, anti-inflammatory effect, antihypercholesterolemic effect, hypoglycemic effect, antiulcerogenic effect, hepatoprotective effect.

### RESUME

We held information-analytical study concerning the scientific literature data of common ginger. It was found that the common ginger rhizomes (*Zingiber officinale* Roscoe, Zingiberaceae L.) are known and used throughout the world. In Europe, it is used as a spice, food product, and is used in medicine. The healing properties of ginger have long been known in the East, and its spectrum of pharmacological activity and use in national health systems is unusually wide. The chemical composition of ginger rhizomes is well investigated by now: the biologically active substances that enhance the basic pharmacological effects are zingerone, gingerols and shogaols ((6)-shogaol). According to preclinical and clinical studies conducted in many countries, the ginger rhizome has a positive effect on the condition and functioning of almost all organs and systems of the body, has anti-inflammatory, expectorant, hypoglycemic, antihypercholesterolemic, antiulcerogenic and hepatoprotective action. It is effective in complex therapy of such socially significant diseases as diabetes and nervous system diseases. At present in Russia the quality of the ginger rhizomes is regulated by standard GOST 29046-91 "Spices. Ginger. Specifications", pharmacopoeia monograph for ginger rhizome is developed, it is adapted to meet the modern requirements for quality standards of crude herbal drugs. Conclusion: The rhizome of ginger is a valuable crude herbal drug that is promising for the development of effective and safe domestic drugs. antihypercholesterolemic, antiulcerogenic and hepatoprotective action. It is effective in complex therapy of such socially significant diseases as diabetes and nervous system diseases. At present in Russia the quality of the ginger rhizomes is regulated by standard GOST 29046-91 "Spices. Ginger. Specifications", pharmacopoeia monograph for ginger rhizome is developed, it is adapted to meet the modern requirements for quality standards of crude herbal drugs. Conclusion: The rhizome of ginger is a valuable crude herbal drug that is promising for the development of effective and safe domestic drugs. antihypercholesterolemic, antiulcerogenic and hepatoprotective action. It is effective in complex therapy of such socially significant diseases as diabetes and nervous system diseases. At present in Russia the quality of the ginger rhizomes is regulated by standard GOST 29046-91 "Spices. Ginger. Specifications", pharmacopoeia monograph for ginger rhizome is developed, it is adapted to meet the modern requirements for quality standards of crude herbal drugs. Conclusion: The rhizome of ginger is a valuable crude herbal drug that is promising for the development of effective and safe domestic drugs. At present in Russia the quality of the ginger rhizomes is regulated by standard GOST 29046-91 "Spices. Ginger. Specifications", pharmacopoeia monograph for ginger rhizome is developed, it is adapted to meet the modern requirements for quality standards of crude herbal drugs. Conclusion: The rhizome of ginger is a valuable crude herbal drug that is promising for the development of effective and safe domestic drugs. At present in Russia the quality of the ginger rhizomes is regulated by standard GOST 29046-91 "Spices. Ginger. Specifications", pharmacopoeia monograph for ginger rhizome is developed, it is adapted to meet the modern requirements for quality standards of crude herbal drugs. Conclusion: The rhizome of ginger is a valuable crude herbal drug that is promising for the development of effective and safe domestic drugs. At present in Russia the quality of the ginger rhizomes is regulated by standard GOST 29046-91 "Spices. Ginger. Specifications", pharmacopoeia monograph for ginger rhizome is developed, it is adapted to meet the modern requirements for quality standards of crude herbal drugs. Conclusion: The rhizome of ginger is a valuable crude herbal drug that is promising for the development of effective and safe domestic drugs.

**Keywords:** common ginger, gingerols, shogaols, expectorant effect, anti-inflammatory effect, antihypercholesterolemic action, hypoglycemic effect, antiulcerogenic effect, hepatoprotective effect.

The traditions of using ginger rhizomes go back to the distant past - up to several thousand years BC. It was an important trade item, it was used as a spice, and its medicinal properties were also discovered.

The first mention dates back to about 2700 BC. One of the three yellow emperors

Shen Nong, described medicinal ginger in his Compendium of Materia Medica on medicinal plants.

Ginger was known in Ancient Egypt, it is mentioned in the largest ancient library of Assyria in 650 BC.

Confucius, in the 5th century BC, discovered the miraculous effects of ginger and recommended it after every meal to aid digestion.

Ginger got to Greece thanks to Alexander the Great (Macedonian), who in 332 BC. conquered Egypt and brought the rhizome of ginger.

The use of ginger is described in the writings of Galen and Dioscorides ("De Materia Medica"). In the Middle Ages, ginger was used as a remedy against the plague, which, if it could not cure, then helped to mitigate the course of the disease.

In the 17th and 18th centuries in Europe, ginger was undeservedly forgotten in favor of other spices, tea and coffee and began to be actively used only in England of the 19th century as a spice in marmalade, cookies, etc., as well as in the 60s of the 19th century. in Germany.

In the 20th century in Europe, ginger rhizomes began to be widely used in medicine and as a spice; at present, this medicinal plant raw material is well studied both from the point of view of pharmacology and phytochemistry. In a number of countries, this is the official medicinal plant material. Nevertheless, the study of the complex of biologically active substances of ginger rhizomes continues, as well as the discovery of its new pharmacological effects.

The purpose of this study: to analyze the data of scientific domestic and foreign literature on the study and scientific evidence of pharmacological effects, validity of use in medicine, modern data on the chemical composition and standardization of rhizomes of medicinal ginger.

Research method: information and analytical.

## results

### I. Botanical and pharmacognostic characteristics

The ginger family (Zingiberaceae) includes 47 genera and about 1000 species. Plants of the ginger family are native to Southeast Asia, China and Western India. The name of medicinal ginger comes from the ancient Roman word Zingiber - "horny" and the Latin officinale - pharmacy (medicinal). In Indian medicine (in Sanskrit), ginger is called "Viśvabheṣaja", which means "the medicine of the world" [3, 4, 10].

Pharmacy ginger (medicinal, real) - Zingiber officinale Roscoe, Zingiberaceae L. is a perennial herbaceous reed tropical plant with a complex root system. The appearance of the plant is described in great detail in the scientific literature of many countries; does not occur in the wild; it is known as a cultivated plant [1, 2, 3, 10].

Ginger blooms in May, the fruits ripen in August. Ginger rhizomes are harvested at the end of the growing season [3].

### II. Spreading

Ginger is cultivated in many countries of the tropical zone: in India, Australia, etc. [1]. Although ginger is native to the humid regions of South Asia, this spicy and medicinal crop is now widely grown in the tropics (for example, India, China, Jamaica, Haiti and Nigeria, Mexico, Hawaii). Jamaica is the largest exporter of this crop. This country exports ginger to all parts of the world - more than two million pounds annually. More than 100 thousand tons of ginger rhizomes are harvested in India, which is half of its world production. Ginger is widely cultivated in Indonesia, Japan, Australia [3, 10]. It is imported to Russia as a spice seasoning [3].

As a medicinal plant raw material and a spice, they use exclusively cultivated plants. Ginger is cultivated in moist, humus-rich soils. Propagated exclusively by dividing rhizomes. It was by rhizomes that it spread throughout the world - now it is grown on almost all continents, with the exception of Antarctica, and even in Europe it has been cultivated since the 17th century in greenhouses and greenhouses [3].

In early spring, pieces of rhizome are planted in fertilized soil and dug out after 6-10 months when the leaves begin to turn yellow and die off. According to the Ayurvedic Pharmacopoeia of India, the harvesting of rhizomes is carried out in January-February. The collected material is thoroughly washed and cleaned from the crust,

then they are soaked for 24 hours and dried in the sun [1, 4].

There are two types of raw materials - black and white ginger. Black ginger is prepared by pouring boiling water over fresh rhizomes without removing the cork. To obtain white ginger, the rhizomes are cleaned and treated with a 2% solution of bleach or sulfuric acid for 6 hours [10].

### III. Characteristics of raw materials

Collected after flowering, cleared of soil, roots, sometimes from cork, cut into pieces and dried rhizomes of cultivated ginger are used as medicinal raw materials and medicines [10].

In addition to dried rhizomes (*Rhizomata Zingiberis*), fresh rhizomes (*Rhizomata Zingiberis recentis*) and the skins of fresh rhizomes (*Cortex Zingiberis recens*) can be used as raw materials. The Ayurvedic Pharmacopoeia of India included an article on ginger rhizomes, peeled from cork and treated with lime [3, 4].

In the works of Russian scientists, the external and anatomical and diagnostic signs of ginger rhizomes are characterized [3, 10].

#### External signs of raw materials

Rhizomes peeled from white cork or unpeeled with annular leaf scars. They are branched, strongly flattened from the sides. Red-brown dots are clearly visible on the cut.

Untreated: the rhizome is compressed laterally, has bridges, oblique branches on the upper side, sometimes has a crack at the top. Whole rhizomes are 5 cm to 10 cm long, 1.5 to 3 cm or 4 cm wide and 1 cm to 1.5 cm thick, sometimes divided longitudinally. The surface of the rhizomes is wrinkled, yellowish or pale to dark brown, more or less covered with cork, which has noticeable narrow longitudinal and transverse ribs; the plug is easily peeled off the side surfaces, but remains between branches. The fracture is smooth, granular with noticeable fibers. On a flat cross-section, a narrow cortex is visible, separated by the endoderm from the central axial cylinder, which is much wider; the rhizome has numerous fibrous vascular bundles and oil cells with yellow content. Moreover, the unpeeled rhizome has an outer layer of dark brown cork. The taste is pungent. The smell is aromatic [3, 7].

Peeled: they differ in that the surface of the rhizomes is smooth, has a longitudinal groove and random loose fibers, light brown in color [3].

It should be noted that the external characteristics of ginger rhizomes can vary depending on the country from which they are obtained. Certain species differ from each other not only externally, but also in color, taste and smell.

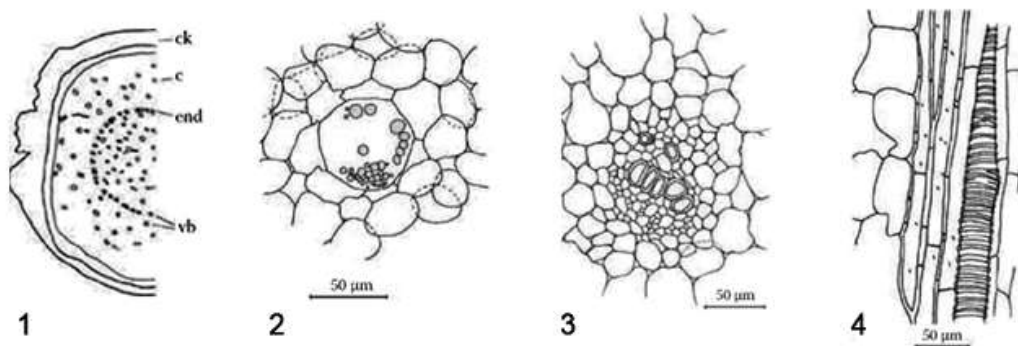
#### Microscopic signs of raw materials

In the literature there are works devoted to the study of the anatomical structure of ginger rhizomes. The following features are characteristic of the rhizome: sparse parenchyma with large oval-shaped starch grains; secretory cells with essential oil, closed collateral vascular bundles, xylem vessels with spiral and scaled type of secondary thickening [3].

Anatomical diagnostic signs transverse cut rhizomes very in detail characterized in the Ayurvedic Pharmacopoeia of India: on the cross section of the rhizome, a bark is visualized, consisting of isodiametric thin-walled cells of the parenchyma, randomly arranged vascular fibrous bundles and numerous isodiametric idioblasts with a diameter of 40-80 microns, containing a resin from yellowish to reddish-brown color. The endoderm is slightly thickened, immediately inside of it there are thin-walled parenchymal cells devoid of starch, among which are randomly scattered collateral vascular fibrous bundles consisting of non-lignified reticular or spiral vessels about 70  $\mu\text{m}$  in diameter, groups of phloem cells, thin-walled septate fibers about 30  $\mu\text{m}$  in diameter, conducting beams 600  $\mu\text{m}$  wide, randomly arranged; elongated porous idioblasts with a narrow cavity (sclereids) and similar to those in the cortex, idioblast cells with resinous contents ranging in length from 8–20  $\mu\text{m}$  to 130  $\mu\text{m}$ . In the longitudinal section, the cortex and the central axial cylinder are visualized with conducting bundles surrounded by rounded-rectangular parenchymal cells with oval starch grains, as a rule, from 5–15  $\mu\text{m}$  to 30–60  $\mu\text{m}$ , with 5 transverse grooves (Figs. 1 and 2) [4].

The European Pharmacopoeia (as well as the British Pharmacopoeia, State Pharmacopoeia

Republic of Belarus, State Pharmacopoeia of China) included microscopy of ginger rhizome powder. When viewed under a microscope crushed raw materials (from pale yellow to brownish color) using a solution of chloral hydrate are visible: groups of large thin-walled cells; rather large vessels with reticular thickenings, often accompanied by narrow thin-walled cells containing brown pigment; profuse thin-walled parenchyma; some cells contain brown oil. Fragments of brown cork are usually visible from the surface (Fig. 3) [4].



Rice. one.1 - Cross section of ginger rhizome: cork from two layers (ck), bark (c) of endoderm (end) and vascular bundles (vb). 2 - Essential oil in parenchyma cells (TS). 3 - Vascular fibrous bundle in bark (TS). 4 - Vessels with annular thickening (LS). TS - tangential section (transverse). LS - lateral section (longitudinal) [4]

#### IV. Chemical composition

Ginger rhizomes contain at least 4.5% of extractives extracted with 90% alcohol, and at least 10% of extractives extracted with water [18, 19, 20].

The rhizomes of ginger contain many substances, the content and percentage of which depends on the growing conditions of the plant and the quality of raw materials: fresh or dried.

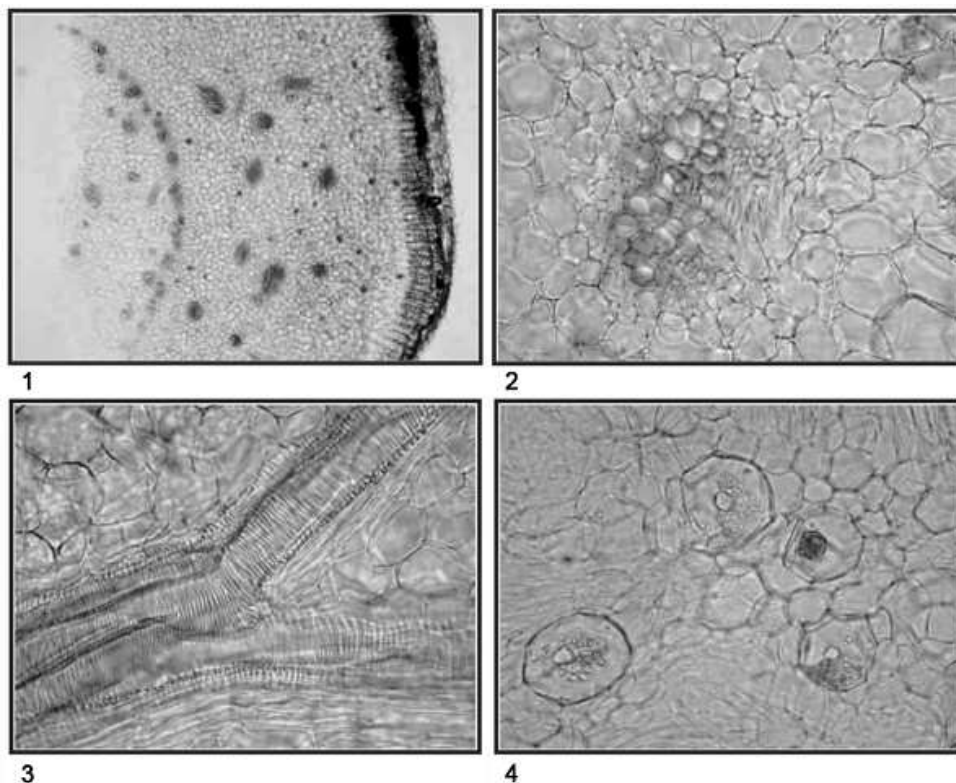
The content of essential oil in ginger rhizomes (1-3%) is significant, the main part of which is sesquiterpenes (zingiberenes, farnesene), terpenes ( $\alpha$ -felandrene, borneol, camphene, geraniol, bornyl acetate, pinenes)), terpene alcohol (linalool), terpenes aldehydes (citral, nonanal), sesquiterpenoids ( $\alpha$ -,  $\beta$ -, --bisabolene),  $\beta$ -sesquifellandrene,  $\beta$ -sesquifellandrol, diterpenes, sesquiterpene alcohol (farnesol), 4-aminobutyric acid.

More than 60 components have been isolated and identified from the essential oil; it is believed that it is the essential oil that provides the main pharmacological effect of ginger rhizomes and its use in traditional medicine. It was found that during the drying process the content of monoterpenes decreases and the amount of sesquiterpenes increases [2, 41].

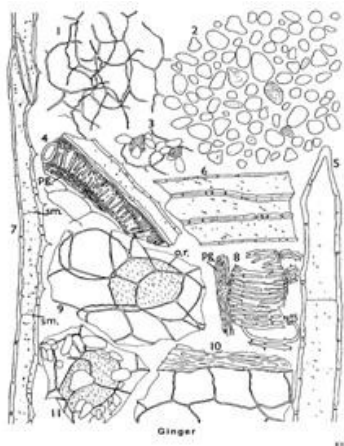
Ginger rhizomes contain numerous ketones (zingerol (zingerol), 6-shogaol, [6] - gingerol, 1- (4-hydroxy-3-methoxyphenyl) octanedione-3,5, [6] -gingerdione, [10] -gingerdione, 1,2-dehydro- [6] -gingerdione; dehydro- [10] -gingerdione; hexahydrocumin, [6] -gingerdiol, [8] -gingerdiol, methylgingerdiol; 4- (3,5-diacetoxyoctyl) -2-methoxyphenol), [6] -gingerdiol-3,5-diacetate; 4  $\gamma$ -o-methyl- [6] -gingerdiol-3,5-diacetate), various paradols (5-deoxygingerols) (Fig. 4) [2, 40].

The burning taste of the rhizome is due to the resinous part known as "gingerol", which is a mixture of different zingerols (gingerols) - 5-8%. A gummy residue can be obtained by extracting the rhizomes with acetone and then evaporating the solvent. Its content ranges from 4-7.5% in dry and up to 20% in fresh ginger rhizomes.

Gingerols are formed at elevated temperatures during drying and storage [2, 41]. The conversion of 6-gingerol to 6-shogaol is pH dependent. The greatest stability of gingerol is established at pH 4, while at pH = 1 and at 100 ° C, a very rapidly reversible transformation occurs (elimination of a water molecule). At higher temperatures, gingerols undergo thermal degradation into gingerones, shogaols, and other related compounds [2, 41].

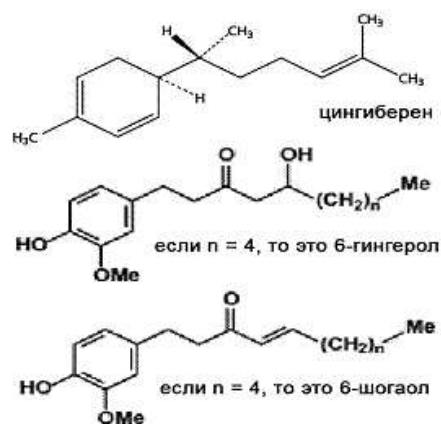


Rice. 2.1 - Cross section of ginger rhizome: cork (two layers), bark, endoderm and central axial cylinder with randomly located fibrous vascular bundles. 2 - Vascular fibrous bundle in the cortex (TS). 3 - Spiral vessels (LS). 4 - Secretory cells (TS) [11].



Rice. 3. Microscopy of ginger rhizome powder (51). 1 - cells of the parenchyma; 2 - starch grains; 3 - a fragment of the parenchyma with idioblast cells (with essential oil) and starch grains; 4 - fibers, parenchyma, vessels; 5 - part of the fiber; 6 - a fragment of a group of fibers; 7 - septic fibers; eight - ladder vessel; 9 - a fragment of the parenchyma with idioblast cells (with essential oil); 10 - obliterated cells of the parenchyma; 11 - a fragment of the parenchyma with idioblast cells (with ether butter) and starch grains.

Lipids (6-8%), capsaicin, caffeic acid, curcumin, amino acids, including essential ones (tryptophan, threonine, leucine, methionine, phenylalanine, valine, etc.), vitamins (nicotinic acid, beta-carotene and vitamin A), up to 50% starch [3, 10, 16, 18, 26, 27].



Rice. 4. The main components of the rhizome of medicinal ginger are zingiberen, 6-gingerol and 6-shogaol [18, 26, 27, 41].

The lipid complex contains free fatty acids (palmitic, oleic, linoleic, etc.); triglycerides, phosphatidic acid, lecithins; ginger glycolipids A, B and C [18].

Proteins, fats, carbohydrates, fiber, potassium, sodium, zinc are also found in the rhizomes of ginger [3]. The study of the qualitative composition of phenolic compounds of ginger rhizomes carried out by domestic researchers by HPLC method made it possible to identify 7 substances: luteolin-7-glycoside, gallic acid, caffeic acid, chlorogenic acid, hyperoside, ferulic acid, 6-gingerol. Flavonoids are present in trace amounts [3].

According to foreign researchers, catechin, epicatechin, naringenin, rutin, quercetin, kaempferol were identified by HPLC in ginger rhizomes, the total content of flavonoids in fresh ginger rhizomes varied from 0.06 to 0.09% depending on the variety and age [48] ...

When studying carbohydrates and organic acids by HPLC, the following sugars were identified in the ginger rhizome: lactose, glucose, galactose; organic acids: oxalic, succinic [3].

Domestic researchers determined: the amount of organic acids - 0.75%, the content of essential oil (2.04%), tannins - 1.96%; polysaccharides in terms of glucose - 18%, the sum of phenolic compounds (spectrophotometrically in terms of 6-gingerol) about 2.3% [3].

The content of ascorbic acid is 45.68 mg / 100 g of ginger rhizome, which is 2 times higher than the corresponding value for apples and is commensurate with the content of ascorbic acid in citrus fruits [16].

At present, an active study of extracts of ginger rhizomes, made with the use of various extractants and promising for the production of medicines, dietary supplements, and use in the perfumery and cosmetic industry, is being carried out [47].

#### V. Pharmacological properties

Medicinal ginger has a wide spectrum of pharmacological activity. It has an antioxidant, tonic, diaphoretic, analgesic, expectorant, antiemetic effect, enhances digestion, stimulates the formation of gastric juice, eliminates stomach and intestinal cramps, is used for malaise and nausea in the morning, as a remedy for headaches, improves appetite. The latest research points to the extremely beneficial effect of ginger on the control of metabolism in the body, due to the distinctive properties of its biologically active substances. Ginger strengthens memory, enhances sexual potency, improves liver function, improves appetite and stimulates digestion, has a carminative effect. It is successfully used to treat various psycho-emotional disorders: fear,

According to the literature, ginger dilates blood vessels, reduces blood viscosity, lowers cholesterol levels, and stimulates cardiac activity. Ginger preparations have

anti-inflammatory effect. It activates digestion, improves bile secretion, relieves intestinal spasms. Ginger rhizomes contain a complex mixture of pharmacologically active substances. 6-gingerol and 6-shogaol contained in ginger exhibit antipyretic, analgesic, anti-inflammatory, antitussive and hypotensive activity. The results of in vitro studies indicate that the active substances that make up ginger are capable of inhibiting the metabolism of arachidonic acid by both the cyclooxygenase and lipoxygenase pathways, i.e. act on the principle of non-steroidal anti-inflammatory drugs (NSAIDs) [3, 18, 26, 27].

According to foreign sources, ginger rhizomes have hypoglycemic, antihypercholesterolemic, antiulcerogenic (gastroprotective) and hepatoprotective effects, inhibit the synthesis of prostaglandins, but all these data require further research. The use of ginger for the prevention of motion sickness is controversial. It is likely that ginger can act locally in the gastrointestinal tract, rather than having a central effect [18, 26, 27].

Clinical studies have focused mainly on the effects of ginger in preventing nausea and vomiting, as well as anti-inflammatory effects [13, 18].

#### In vivo and in vitro studies

In vitro studies have demonstrated that the biologically active substances of ginger, 6-, 8- and 10-gingerols and galanolactone, have antiserotonergic activity [18].

#### Antiemetic activity and action on the digestive system

In the scientific literature there are examples of studies documenting the antiemetic activity of ginger extract in vivo (eg, in dogs, rats, mice, leopard and true frogs) [13, 18, 26, 27].

The antiulcerogenic effect of ginger extract (acetone) and cingiberin on gastric damage caused by hydrochloric acid has been shown in rats and rabbits [13, 18, 26, 27].

Antiplatelet activity. 6-gingerol, 6- and 10-dehydroingerdione, 6- and 10-gingerdione, potent inhibitors of prostaglandin (PG-synthetase) biosynthesis in vitro, were more potent than indomethacin. Concentration-dependent inhibition of in vitro platelet aggregation induced by (ADP), adrenaline, collagen and arachidonic acid has been described for an aqueous extract of ginger. Ginger was also found to reduce aggregation of prostaglandin-endoperoxide, thromboxane and prostaglandins. A good correlation has also been reported between the concentration of the extract required to inhibit aggregation and the concentration required to inhibit thromboxane synthesis in platelets [18, 27].

Anti-atherosclerotic and antioxidant activity. Orally administered ginger essential oil inhibited increases in liver and serum cholesterol in rats, reducing cholesterol absorption. Antihypercholesterolemic activity was also recorded for dried ginger rhizomes, in mice, rats and rabbits on a cholesterol-rich diet and with existing hypercholesterolemia. However, fresh ginger juice was found to have no effect on serum cholesterol concentrations 4 hours after administration. In addition, serum cholesterol concentrations were not increased at all within four hours after cholesterol administration [18, 26, 27].

In the works of Russian scientists, the integral antioxidant activity of various ginger extracts was investigated using electrochemical detection and its dependence on storage conditions. It was found that the antioxidant activity of the aqueous-alcoholic extract of ginger is approximately 1.5 times higher than the corresponding value for the aqueous [17, 40].

#### Anti-inflammatory activity

It was found in vitro (in a study on intact human lung epithelial cells (A549 cells), on a chorioallantoic membrane model of a chicken embryo) and in rats with chronic simulated adjuvant arthritis that biologically active substances of ginger have anti-inflammatory activity [18].

#### Antiviral activity

In vitro experiments have shown the activity of sesquiterpenes isolated from ginger rhizomes,

against rhinovirus IB.

#### Anticancer activity

In vitro and in vivo experiments have shown the chemopreventive, cytotoxic, or cytostatic activity of extracts of ginger and ginger BAS [26, 27].

In in vitro experiments, incubation of 6-gingerol with human promyelocytic leukemia cells (line HL-60) led to inhibition of cell viability and DNA synthesis. Microscopic examination of these cells indicated the induction of apoptosis by 6-gingerol [18, 26, 27].

#### Other types of pharmacological activity

In experiments on rats, the tranquilizing activity of combinations of standardized extracts of ginger and ginkgo biloba, which were administered intragastrically at doses ranging from 0.5 to 100 mg / kg, was assessed in the "elevated cruciform maze" test. The combination was found to have a tranquilizing effect at lower doses and anxiogenic effect at higher doses.

For the juice of fresh ginger rhizomes administered orally, a hypoglycemic effect was found on healthy rabbits and rats with alloxan diabetes. The effect was significant in diabetic animals.

The potential efficacy of ginger rhizomes and its individual components in reducing insulin resistance and the possibility of treating type 2 diabetes and prediabetes was demonstrated in rats using a high-calorie, high-carbohydrate diet model [14].

Comparison of the pharmacological activities of 6-shogaol and capsaicin showed that both substances caused rapid hypotension in rats after intravenous administration, accompanied by a marked vasopressor response, bradycardia and dyspnea. The vasopressor response was thought to have a centrally acting mechanism.

Contraction of isolated guinea pig trachea from both substances, positive inotropic and chronotropic responses in isolated rat atria to 6-shogaol, were thought to be caused by exposure to an unknown active substance on nerve endings. A powerful positive inotropic effect has been found on isolated guinea pig atriums (atria), and the cardiotoxic effect of gingerols has been proven.

In experiments on rats, the choleric effect of acetone extract of ginger, administered intraduodenally, was described. 6-Gingerol and 10-gingerol were reported to be more active ingredients, causing a significant increase in bile secretion even four hours after administration [18].

The nephroprotective effect of ginger has been established (shown in mice when exposed to cisplatin), hepatoprotective action has been shown in rats when exposed to carbon tetrachloride, larvicidal action - shown to be an action against *Angiostrongylus cantonensis* (the most common cause of eosinophilic meningitis in Southeast Asia and the Pacific Basin), *Adese aegypti*, and *Culex quinquefasciatus* [40].

The immunomodulatory effect of ginger essential oil, the anthelmintic effect of the aqueous ginger extract against *Pheretima posthuma* and 100% effectiveness of the anthelmintic effect of the methanol extract of ginger against *Haemonchus contortus* [40].

The positive effect of an aqueous extract of ginger rhizomes on reducing the severity of symptoms in complications of Dengue fever has been shown [41].

#### Clinical researches

Clinical studies of ginger have focused mainly on its effects in preventing nausea and vomiting of various origins. Other clinical studies have evaluated the effects of ginger preparations on gastrointestinal motility, thrombogenesis, dizziness (vertigo, vertigo, vestibular vertigo) and inflammation such as osteoarthritis [18, 26, 27, 53].

Ingestion of ginger rhizome powder significantly lowers blood glucose and glycated hemoglobin HbA1c. The efficacy of ginger rhizome powder with proper diet and lifestyle correction in the treatment of type 2 diabetes has been shown [6].

The neuroprotective effect of ginger rhizomes has been established [26, 27].



### Other effects

In a study on 7 women, it was found that oral intake of fresh ginger rhizomes at a dose of 5 g decreased the concentration of thromboxane B2 in the blood serum collected after clotting, which indicates a decrease in the synthesis of eicosanoids (associated with platelet aggregation) [18, 26, 27, 53] ...

Study of the antimicrobial activity of dry pharmacy ginger on international test strains: *Staphylococcus aureus* (ATCC 653 8-P), *Pseudomonas aeruginosa* (ATCC 9027), *Escherichia coli* (ATCC 25922), *Candida albicans* (ATCC 885-653), (10702) showed moderate antibacterial activity [3].

The essential oils of fresh and dried rhizomes of *Zingiber officinale* were analyzed using gas chromatography. It was found that the main component of both oils was cingiberen. In the essential oil of fresh rhizomes, the second main component was geranial (8.5%), and the content of oxidizable substances was higher (29.2%) compared to the essential oil of dried rhizomes (14.4%). The essential oil of dried ginger rhizomes also contained  $\alpha$ -curcumin (11%),  $\beta$ -bisabolene (7.2%), sesquivellandrene (6.6%), and  $\delta$ -cadinene (3.5%). Antibacterial activity of oils against *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Candida albicans*, *Trichoderma* spp., *Aspergillus niger*, *Penicillium* spp. and *Saccharomyces cerevisiae* were evaluated by disc diffusion. It was found that the minimum overwhelming concentration of oils ranged from 10  $\mu\text{g} / \text{ml}$  to 1  $\mu\text{g} / \text{ml}$ , which is very significant. Research has shown the possibility of using ginger essential oil in the treatment of many bacterial and fungal diseases [21, 26, 27, 53].

### Side effects, toxicity

#### Preclinical data

Shown low toxicity of ginger oil in an acute toxicity study with an LD50 (rat, oral; rabbit, dermal) exceeding 5 g / kg.

Mutagenic activity was found for an alcoholic extract of ginger, gingerol and shogaol on *Salmonella typhimurium* strains TA100 and TA1535 with exogenous metabolic activation (compound S9), but not in TA98 or TA1538, with or without compound S9.

Zingerone was found to be non-mutagenic for all four strains with or without S9 and was reported to suppress the mutagenic activity of gingerol and shogaol. Ginger juice has been reported to show anti-mutagenic activity, while mutagenic activity has been described for 6-gingerol in the presence of known chemical mutagens. It was hypothesized that certain mutagens could activate the mutagenic activity of 6-gingerol so that it was not suppressed by the antimutagenic action of the juice components [18].

#### Clinical trial data

No side effects have been reported. However, there is a paucity of data on toxicity and clinical safety, and further research on ginger is required in this aspect. Ginger oil has been claimed to be non-irritating and non-sensitive, although hypersensitive individuals may have dermatitis. Phototoxic reactions are not considered significant.

### Toxicity

Ginger is classified as a natural food additive by the Council of Europe (category N2), and was previously recognized by the FDA as safe (GRAS) [18].

There have been no reports of allergic reactions to ginger, but there is evidence of contact dermatitis in occupationally exposed persons [25].

There are no potentially toxic compounds in ginger.

Acute toxicity: In addition to mild dyspepsia in individuals not accustomed to spicy foods, no acute toxicity has been found at usual doses for nutrition or medicinal purposes. Very large doses (6 grams or more of ginger) can irritate the stomach [26].

In usual doses (up to 2 g per day), ginger has no effect on blood clotting or any other coagulation parameters [27, 28, 29].

When studying the acute toxicity of the essential oil of ginger rhizomes in rats, the LD50 was more than 5 grams of ginger oil per kilogram of animal weight [30].

Chronic toxicity: not reported, no significant mutagenic or carcinogenic effects [31, 32].

The alleged safety is based on a long history of use as a food product.

There were no data on side effects during pregnancy. However, due to the available data on uterotonic activity (causing muscle spasm of the uterus) of a related species, *Zingiber cassumunar*, some authors recommend avoiding ginger during pregnancy [18, 33, 34, 42, 43].

#### Vi. Medications

Ginger rhizomes are widely used in medical practice worldwide. In the Russian Federation, 14 drugs are registered as medicines: there are both preparations only from ginger rhizomes, and complex medicines, which include, along with extracts or tincture of ginger, extractive preparations from other types of medicinal plant materials, as well as chemical and pharmaceutical substances (Table 1).

It is obvious that preparations containing the rhizomes of medicinal ginger per se or in the form of extracts are approved for medical use as herbal medicines that are expectorant, anti-inflammatory, antiseptic, improving digestion and metabolic processes. [45].

Table 1

Medicines from the rhizomes of medicinal ginger

Drug name, release form	Manufacturer	Pharmacotherapeutic group
<b>one-component preparation</b>		
AVIOPLANT capsules (powder of ginger rhizomes)	Fitofarm Klenka AO, Poland	Herbal antiemetic
<b>multicomponent preparations</b>		
VITRUM® BEAUTY ELITE tablets p / o (extract of medicinal ginger rhizomes)	Unipharm Inc., USA	Multivitamin + other preparations
DOCTOR MOM® syrup (dry extract of medicinal ginger rhizomes)	Unique Pharmaceutical Laboratories (a division of JB Chemicals & Pharmaceuticals Ltd.), India	Expectorant vegetable origin
DOCTOR MOM® herbal lozenges, for cough (dry extract of medicinal ginger rhizomes)	Unique Pharmaceutical Laboratories (a division of JB Chemicals & Pharmaceuticals Ltd.), India	Expectorant vegetable origin
ZINAXIN capsules (extract of medicinal ginger rhizomes)	FERROSAN, A / S, Denmark	Anti-inflammatory herbal remedy origin
Klosterfrau Melisana elixir (essential oil of medicinal ginger rhizomes)	MKM Klosterfrau Fertriebs GmbH, Germany	Sedative vegetable origin
Maraslavin solution for local use (decoction of medicinal ginger rhizomes)	Sopharma JSC, Bulgaria	Herbal antiseptic
MULTIPRODUCT FOR MEN effervescent tablets (extract of rhizomes of medicinal ginger)	Natur Product Europe B.V., The Netherlands	Multivitamin + other preparations
Bittner's original large balm, oral and external balm	Richard Bittner AG, Austria	General tonic herbal remedy
RUMALAYA tablets (extract of rhizomes of medicinal ginger)	Himalaya Drag Co, India	Anti-inflammatory means
SODEKOR tincture (rhizomes of medicinal ginger)	JSC "Pharmaceutical Factory of St. Petersburg", Russia	General tonic herbal remedy
Suprima-Broncho syrup (thick extract of medicinal ginger rhizomes)	SHREYA LIFE SCIENCES Pvt. Ltd., India	Expectorant vegetable origin
TRAVISIL tablets for sugar-free resorption (extract of rhizomes of medicinal ginger)	PLETHICO PHARMACEUTICAL, Ltd. (India)	Expectorant vegetable origin
Fitolor herbal pastilles (extract of medicinal ginger rhizomes)	Marichi Exports Pvt. Ltd, India	Expectorant vegetable origin

In addition, a significant number of preparations containing ginger have been patented in the world [18]. The rhizomes of medicinal ginger (in the form of powder, hydroalcoholic extracts, essential oil) are an active component of a large number of dietary supplements that are recommended as anti-inflammatory (for example, for the treatment of joints) and many other agents.

#### Vii. Application

In official medicine, ginger is used as a carminative, diaphoretic and antispasmodic agent: for intestinal colic and dyspepsia, accompanied by flatulence. It is currently used to prevent nausea and vomiting, especially during motion sickness, as a means of improving digestion, and as an anti-inflammatory agent in the complex therapy of diseases such as osteoarthritis and rheumatoid arthritis [18].

#### Recommended dosage of ginger rhizomes

Dosages are indicated for oral use with traditional use recommended by standard herbalists:

Rhizome powder 0.25-1 g, three times daily.

Tincture 1.5-3 ml (1: 5) three times daily, 1.7-5 ml daily (according to various literature)

[eighteen].

Adults: There is disagreement on the optimal form of use and dosage of ginger. For dried rhizomes, from 250 mg four times a day orally [33] (England) to 1 g four times a day orally [38] (Germany), and 2.5 g four times a day orally (China).

Pediatric dosage is unknown.

As an antiemetic, ginger rhizome powder is taken once in an amount of 1-2 g 30 minutes before travel to prevent seasickness, or 0.5 g, 2-4 times daily.

The use of rhizomes of medicinal ginger in folk medicine of the countries of the world The history of the use of ginger as a spice and medicine comes from ancient times. In East Asian countries, crushed ginger rhizomes are prescribed for neuralgic and spasmodic headaches, bronchial asthma [1, 3, 10].

Ginger is widely used in Ayurvedic medicine and traditional Chinese medicine to eliminate headaches, normalize the functions of the gastrointestinal tract, for joint diseases (anti-inflammatory), and acute respiratory infections. According to literary sources, ginger dilates blood vessels, reduces blood viscosity, prevents platelets from sticking together, which reduces the risk of heart attack, lowers cholesterol levels, stimulates cardiac activity and metabolic processes, lowers temperature in inflammatory processes, is effective for the prevention and treatment of migraine, with toothache, in the treatment of various diseases of the ENT organs and the respiratory tract of an inflammatory nature, has a hypotensive effect, ginger rhizomes are part of the TCM recipe recommended for the treatment of epilepsy [3, 10, 16, 18, 26, 27, 40, 49,

In traditional Chinese medicine, the properties of ginger are: a pungent, dry, Yang herb, which is used to treat diseases caused by cold, damp weather [36]. In Arabic medicine, ginger is considered an aphrodisiac [35].

#### Ginger oil

Essential ginger oil is widely used in cosmetology, aromatherapy, massage, baths and compresses. When applied externally, ginger oil has a warming effect on soft tissues, increases blood circulation, relieves muscle and joint pain. When taken internally, the oil has an antipyretic and analgesic effect, increases appetite and normalizes digestion. Vapors of ginger essential oil, when used in aroma lamps, have a calming effect, raise mood, and act as an antiseptic during outbreaks of influenza and acute respiratory infections. When using ginger oil, it should be diluted 1: 2 with other more neutral oils, such as linseed oil.

When making solutions consume ginger root for medicinal purposes, should

consult with your doctor about the compatibility of this product with the current condition of the disease. Also, ginger, when used with drugs, can enhance their effect and cause irreparable harm to the body.

#### Contraindications

In total, ginger is low-allergenic in its properties and has practically no contraindications. Ginger tea is contraindicated for pregnant women in the second trimester, hypertensive patients during a crisis and people during an exacerbation of gastrointestinal diseases. Due to the high concentration of substances, essential oil is contraindicated in children under seven years of age. Ginger in any of its forms is contraindicated for people with impaired renal and urinary tract function, inflammatory processes, as well as when sand or stones are detected in them, with various kinds of bleeding and hepatitis.

#### VIII. Ginger rhizome standardization

Currently in Russia the quality of ginger rhizomes is regulated by GOST 29046-91. Spices. Ginger. Technical conditions.

This standard applies to the spice - ginger, which is the dried peeled rhizomes of the tropical plant *Zingiber officinale* Rosc. (from the ginger family), used in the preparation of various food products.

The requirements of this standard are mandatory. Quality indicators include appearance, color, aroma and taste, physical and chemical indicators (% , no more): mass fraction of moisture, mass fraction of ash, mass fraction of essential oils, mass fraction of rhizomes with a coarse fiber structure and a darkened core, mass fraction of affected rhizomes surface mold visible to the naked eye, mass fraction of damaged rhizomes, grind size: mass fraction of product coming off a wire mesh sieve N 095, mass fraction of product passing through a sieve of wire woven mesh N 045, mass fraction of metal impurities (particles not more than 0.3 mm in the largest linear dimension), pest infestation of grain stocks and foreign impurities and rotten rhizomes are not allowed.

The content of toxic elements and pesticides is regulated.

There is no domestic regulatory documentation for ginger rhizomes for medical use.

At present, the draft FS "Pharmaceutical ginger rhizomes" and the draft FS "Dry pharmacy ginger extract" have been developed, but not approved. The draft of the Pharmacopoeia Monograph (FS) "Ginger of the medicinal rhizome" was developed at the First Moscow State Medical University. THEM. Sechenov [3].

The project was drawn up and executed in accordance with the requirements of OST 91500.05.001-00 and OST 42-3-84. According to the draft FS "Pharmaceutical ginger rhizomes" the authenticity of raw materials is determined by external signs (whole raw materials), microscopy (cross section) and chromatographic identification of gingerol and terpenoids (TLC) is carried out.

Specific indicators of the quality of raw materials of ginger rhizomes include: the content of the sum of phenolic compounds in terms of 6-gingerol [3]. Spectrophotometrically in the UV region, the amount of phenolic compounds is determined in terms of 6-gingerol, which should be at least 2.0%.

Due to the wide spectrum of pharmacological activity, ginger rhizomes have found application in folk and official allopathic medicine in many countries of the world, are used in Ayurvedic medicine in India and in homeopathy.

Normative documentation for ginger rhizomes is included in the European Pharmacopoeia and a number of national pharmacopoeias in the world. An analysis of the quality requirements for the rhizomes of medicinal ginger of the Chinese State Pharmacopoeia, the European Pharmacopoeia, the British Pharmacopoeia, the State Pharmacopoeia of the Republic of Belarus, the Indian State Pharmacopoeia 2010, the Ayurvedic Pharmacopoeia of India and the draft of the domestic FS showed that the authenticity of the rhizomes of medicinal ginger is determined macro- and microscopically, but in some the articles do not characterize either whole or crushed raw materials, as well as chromatographically (with the exception of the Indian Ayurvedic Pharmacopoeia) and as reference samples, either standard samples of resorcinol and citral, or standard extracts of rhizomes of medicinal ginger are used;

Articles of the European Pharmacopoeia, British Pharmacopoeia and State Pharmacopoeia of the Republic of Belarus are harmonized. At a more modern level is the article of the Indian State Pharmacopoeia 2010, which includes the quantitative determination of gingerol by HPLC. It should be noted that the Indian Ayurvedic Pharmacopoeia indicates the medical use and doses of the rhizomes of medicinal ginger in Ayurvedic medicine, as well as the chemical composition (briefly). The completeness of the characteristics of the anatomical and diagnostic features of the rhizomes of medicinal ginger in all pharmacopoeial monographs, with the exception of the article of the Indian Ayurvedic Pharmacopoeia, requires improvement, but the articles of the European and British (2009 and 2013) pharmacopoeias provide a microscopic drawing of the powder of medicinal ginger rhizomes [46, 52].

#### Standardization of ginger rhizomes used in homeopathy

The quality of ginger rhizomes used for the preparation of homeopathic medicines is regulated by the FS, which are part of the German (HAB) and French (FHP) homeopathic pharmacopoeias officially recognized in the European Union. We carried out a comparative analysis of articles of available foreign homeopathic pharmacopoeias on raw ginger used for the preparation of homeopathic medicines - FS HAB and FS FHP. It should be noted that FS HAB is not very informative and refers to FS DAB regarding the requirements for the quality of ginger rhizomes and the method for determining the authenticity of the matrix tincture. The NAB article in ginger rhizomes regulates the content of essential oil (not less than 1.5%), it is indicated that the matrix tincture is prepared in 86% ethyl alcohol according to the method 4a. For matrix tincture, a description of the appearance is given, the relative density (0.825–0.845) and the dry residue (not less than 0.8%) are regulated. Storage conditions are indicated in a dark place. The FS FHP describes in detail the external signs of ginger rhizomes, there is a description of the anatomical and diagnostic signs of a cross section of the rhizome, in addition, the authenticity of the raw material is confirmed chromatographically: thin layer chromatography (TLC) is used (without reference substances), the TLC conditions are indicated in the section on determining the authenticity of the matrix tinctures. For raw materials, "total ash" is regulated (no more than 8%). The matrix tincture is prepared in 65% ethyl alcohol, a description of the appearance is given, and the authenticity is established by light green fluorescence at 365 nm, a qualitative reaction with "Strong blue B" and TLC.

As a result of the information and analytical study, it was established that both FSs include requirements for the quality of medicinal plant raw materials, but the FHP FS includes only the determination of the authenticity of raw materials, and the standardization of matrix tinctures for both FS does not provide for a quantitative determination of the content of active substances, with the exception of the total indicator - dry residue ... It was found that, despite the fact that the raw materials in both articles are dried ginger rhizomes, there are significant differences between the articles in terms of preparation and methods for determining the authenticity and good quality of matrix tinctures [37].

#### Conclusion

Ginger rhizomes are a promising medicinal plant raw material for the development of effective and safe domestic medicines.

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