Alpinia officinalis (Alpinia officinarum). Publication 3: biological action, use in traditional medicine and modern world medical and pharmaceutical practice

T.L. Kiseleva
Professional Association of Natural Therapists (Moscow)

Lesser galangal (Alpinia officinarum). Article 3: Biological activity, use in Traditional medicine and current medical and pharmaceutical practice

TL Kiseleva
Professional Association of Naturotherapists (Moscow, Russia)

SUMMARY

The carried out information-analytical research allowed install proven efficacy and safety of Alpinia officinarum rhizome extracts. The papers describing the mechanisms of action of biologically active substances a. medicinal, as well as processes that cause antitumor and some other established biological effects. It has been shown that, along with high efficiency, some of the studied biologically active substances exhibit selectivity, which allows us to consider them as promising sources for the creation of natural drugs, dietary supplements to food, and SPP. No toxic effects have been identified.

Phenols (flavonoids, diarylheptanoids (DAG), phenylpropanoids), terpenes, phytosterols, and adducts of DAGterpene nature can be considered the main groups of biologically active substances responsible for a wide range of pharmacotherapeutic action of rhizomes of small galangal. The phenolic fraction obtained using various solvents, like individual biologically active substances, including adducts of DAG and terpenes, exhibit pronounced antiproliferative, antioxidant, anti-inflammatory, antiviral, neuroprotective, antiosteoporotic, antiulcer, antihyperlipidemic effects. Terpenes (including diterpenes) are mainly responsible for antimicrobial, anti-inflammatory, antiproliferative, antiviral effects.

The results obtained indicate a high nutraceutical potential and good prospects for the use of alpinia officinalis in the world medicinopharmaceutical practice as a source of drugs, dietary supplements for food and SPP.

Key words: traditional medicine, alpinia officinalis, Alpinia officinarum, flavonoids, diarylheptanoids, phenylpropanoids, terpenes, adducts of DAH-terpene nature, antiviral action, antitumor action, antimicrobial action, antioxidant action, anti-inflammatory action, neuroprotective action.

RESUME

This review presents analysis of biological activity, traditional medicine and current scientific data on use of Lesser galangal (Alpinia officinarum) in medical and pharmaceutical practices. It was shown that based on its successful use in Traditional medicine for centuries, this herb generates significant interest from research laboratories across the globe. We found papers describing the mechanisms of action of biologically active substances (BAS), as well as the processes that cause antitumor and some other identified biological effects of Lesser galangal. It is shown that along with high efficiency, some of the studied BAS exhibit selectivity, which allows us to consider them promising sources for the creation of natural medicines, dietary supplements and specialized food products (SFP). No toxic effects were detected.

The main groups of BAS responsible for a wide range of pharmacotherapeutic effects of Lesser galangal rhizomes are phenols (flavonoids, diarylheptanoids (DAG), phenylpropanoids), terpenes, phytosterols, and DAGterpene adducts. The phenolic fraction obtained with the help of various solvents, as well as individual BAS, including adducts of DAG and terpenes, exhibit significant antiproliferative, antioxidant, antiinflammatory, antiviral, neuroprotective, antiosteoporotic, antiulcer, antihyperlipidemic effects. Terpenes (including diterpenes) are mainly responsible for antimicrobial, antiinflammatory, antiproliferative, and antiviral effects.

In this way obtained results indicate a high nutritional potential and good prospects for the use of Alpina officinalis in the modern medical and pharmaceutical practice as a source of medicines, dietary supplements and SFP.

Keywords: traditional medicine, Lesser galangal, Alpinia officinarum, flavonoids, diarylheptanoids, phenylpropanoids, terpenoids, diarylheptanoidterpene adducts, antiviral effect, antitumor effect, antimicrobial effect, antioxidant effect, antiinflammatory effect, neuroprotective effect.

INTRODUCTION

Medicines (drugs), dietary supplements to food (dietary supplements) and specialized food products (SPP) on

based on plant raw materials are effective, safe and in demand in domestic medical practice. Some unique types of plants and medicinal plant materials have been used for thousands of years - from ancient times to the present. Such "vitality" is historically conditioned not only by the wide distribution of species in nature, sufficient resources and safety, but, first of all, by the unique types of pharmacotherapeutic action of these plants.

The ethnobotanical and ethnopharmacological interest in such plant species on the part of modern representatives of the scientific community is based, inter alia, on economic aspects, since the creation of modern effective and safe herbal preparations, dietary supplements and SPP often allows developing companies to introduce unique in efficiency, but very economical means and methods for the prevention and treatment of even rare and / or socially significant diseases.

Various species of the genus can be safely attributed to the number of plants traditionally used for thousands of years for food and medicinal purposes. Alpinia.

Numerous studies in vitro and in vivo, carried out both for extracts and forindividual connections Alpinia officinarum,testify to a wide range of
pharmacotherapeutic actions, including anti-inflammatory, antibacterial, antifungal, antiproliferative, diuretic, antihyperlipidemic, antioxidant, antiemetic, antiobesity, antiosteoporotic, antitumor, inhibitory enzymes and NO production [43, 55, 87, 193, 193, The established unique antiviral properties look especially promising. medicinal in connection with the emergence of virulent respiratory diseases not only in Asia and the Middle East [173, 178, 193].

This work continues the series of publications devoted to a. medicinal (Alpinia officinarum).Publication 1 was devoted to the characteristics of the research object in terms of its botanical features, synonymy and traditions of food use [19]; publication 2 covers the issues of phytochemistry of rhizomes a. medicinal, including its modern varieties [20].

The purpose of this information and analytical study is to objectify information aboutthe spectrum of biological activity (in comparison with the experience of traditional use) and the prospects for the use of a. medicinal as a source of modern domestic drugs and / or phytonutrients.

MATERIALS AND METHODS

The objects of the research were normative documents recommended for use in the prescribed manner, and bibliographic sources of a high degree of reliability, including monographs, scientific periodicals, reference books, dissertations, dissertation abstracts, as well as electronic scientific and official databases. We also took into account Internet resources with links to bibliographic sources of a high degree of reliability. Keyword search includingA. officinarum and synonyms were carried out using electronic databases, includingISI, Science direct, Scopus, PubMed, Google Scholar and defended dissertation database.

Conventional medical terms are quoted either in quotation marks, in italics, or in capital letters, in accordance with the conventions generally accepted in various traditional medical systems. The synonymy of the investigated species of alpinia is presented in accordance with [19].

When performing the work, the following analytical, historical, methods research: information content analysis, systematization were used.

1. Uses of Alpinia officinarum in Traditional Medicine

In the Middle Ages, the rhizomes of the Lesser Galangal were initially known as a medicine (not a spice), which Arab doctors and "healers" quite widely spread throughout southern Europe [3, 17, 38, 150]. At that time, galanga rhizomes were used as a remedy to strengthen the stomach, relieve colic and stimulate appetite [13]. In addition to rhizomes, galanga oil was also famous and popular [17].

The most famous and influential philosopher and scientist of the medieval Islamic world, Avicenna [92], described small galangal as a stomachic and stimulant agent, useful for phlegmatic people and with stomach moisture. In his opinion, the rhizome promotes digestion due to the heat and secretions that it causes in the stomach, and thereby relieves colic, and also gives flavor to the breath. In addition, it warms the Kidneys, which makes the sperm agitated, and if a piece of rhizome is kept in the mouth, the small galangal causes an erection [207].

O.D. Barnaulov [3, 4] quotes the following from "Odo from Mena" (11th century):“You take galangal and it will immediately dissolve phlegmon in the stomach. If the sick person is phlegmatic, then his strength is strengthened.

When it is taken, it drives out the winds imprisoned
inside, Digestion improves and cures colic.
If you chew it, your mouth will smell pleasant. When taken, it
multiplies the desire and action of the kidneys ”[3, 4, 26].

The German nun and healer Hildegard Bingen (1098-1179) believed that galangal (rhizome A. officinalis) is the best remedy for angina pectoris: “Anyone who finds pain in the region of the heart or suffers from heart failure should immediately consume the right amount of galangal, and then he will recover ”[195]. According to J. Duke (2003), with reference to M. Grieve (1931), the rhizomes of small galangal were also a favorite remedy in Estonia and Lithuania [83].

Nicholas Culpeper (1616-1654) wrote about the “large and small” galangal: “Both are sharp and dry to the extreme, and the“ small ”galangal is considered sharper; it greatly strengthens the stomach and relieves pain caused by exposure to cold or wind; its aroma cleanses the brain, strengthens weak hearts, removes winds from the belly, warms the loins and provokes love yearning. Take half a drachma (from 4 to 7 g) at a time ”[27, 72]. In this case, Culpeper follows J. Gerard (c. 1545-1612), who wrote that both types of galangal are aphrodisiacs, “promote coitus by warming up excessively cold members” [27].

Maino de Manieri Maineri in his treatise "The Rules of Health" (a medieval guide to lifestyle) gave a recipe for "soft-boiled eggs, carefully mashed with cinnamon, pepper, salt, galangal", which "truly strengthens all limbs, especially the ejaculating", since the egg was with fertility, and hot spices - with desire [27]. Constantine the African (between 1010 and 1020-1087) advised the use of galangal in "restorative procedures", taking it after lunch and dinner. Tunisian physician Ibn al-Jazzar (c. 895-c. 979), from whom, according to O'Connell (2015) [27], Constantine borrowed many of his recipes, wrote that galangal can cause "instant erection" [227] ... This is quite consistent with the fact that the Arabs from ancient times fed their horses with a small galangal in order to "make them more passionate and fiery" [83].

In medieval Armenian medicine, small galangal was considered “a root similar to ginger” [2]. “Its nature is hot and dry in the third degree ... Makes pleasant taste in the mouth, improves complexion. Eliminates the smell of onions, wine, garlic from the mouth. Strengthens the stomach, aids in the digestion of food. Helps with colic, stomach pains, kidney diseases ”[2–4].

In oriental medicine, rhizomes have been and are used as an anti-febrile and to relieve abdominal pain [55], chronic enteritis (inflammation of the small intestine), indigestion, and pain in the stomach. It is believed that galanga promotes gas release, prevents relapses in chronic diseases of internal organs, stimulates salivation, and increases the functional activity of the stomach. The rhizome is also used for exhaustion, lack of appetite, headaches with syncope, hypochondria, and motion sickness [47].

O.D. Barnaulov (2015) ironically calls this plant Egyptian ginseng: “In Egypt, the spice traders, overwhelmingly ignorant of what they were selling, declared that shriveled Galant roots with a pungent taste were ginseng,” since a positive effect on potency was put forward as its main action [3].

Describing his own experience in using galangal and illustrating the little popularity of this rhizome in the professional medical community, O.D. Barnaulov writes that one doctor brought him a rhizome from Morocco and convinced the others that it was allegedly Rhodiola rosea. And he was hardly convinced that this was not so, breaking both rhizomes at the same time - neither taste nor color matched. At the same time, the author of the famous "Medicinal properties of spices" [3] notes that in his clinical (phytotherapeutic) practice he rarely and very limitedly uses galanga due to the lack of raw materials.

Modern Brazilian researchers note a wide range of traditional uses of Alpinia officinalis in folk medicine. These rhizomes are used to treat catarrh, rheumatism, halitosis, bronchial ulcers, coughs, throat infections, and digestive problems [230].

In the traditional medicine of Thailand, the rhizomes of a. drug is used to treat cancer [142], as a carminative, antifungal and antipruritic agent [108, 158]. In Malaysia, galangal is also traditionally used to treat cancer [142]. In Ayurvedic and traditional Chinese medicine (TCM) it has been used since ancient times for fairly broad indications [55, 150]. In India small galangal is also used as a deodorant and breath freshening agent [27]. Generally,A. officinarumhas been used for centuries as an antiemetic, gastric and analgesic agent throughout Asia [100, 133].

Also throughout Asia, in Turkey, Morocco and Iran a. medicinal is used in the form of a decoction, infusion, juice in the form of a separate extract or in combination with other medicinal plants (RL), food or

drinks to treat general health problems, including colds, inflammation, indigestion, stomach pain, etc. The plant is also used to treat malaria [43].

Ayurveda. Alpinia officinalis has an Indian nameRasna [15]. In terms of energy, it has: tasteSpicy; virya (thermal effect) warming; vipak (effect after digestion) Pungent.Effects on Doshas: Kapha, Vata, Pita [15, 22]. The pungent taste is most beneficial for Kapha people [22, 36]. According to Ayurvedic concepts, the beneficial effect of the Pungent taste is manifested in improving digestion and cleansing the body. An excess of Acute leads to increased acidity, weight loss, dry tissue, irritability. Its lack is manifested in the weakness of digestion, stagnation, lethargy, the formation and accumulation of ama and mucus [36].

The tropism of Galangalus lesser: alimentary tract [15]. Action: stimulating, diaphoretic, antirheumatic, improving appetite, promoting digestion [15, 22]. Indications: stomach diseases (ulcers, gastritis, colic) [15]. Dosage forms: infusion, decoction [15].

TCM. Historically in China, the rhizomes of a. medicinal is used as a gastric remedy [108], in particular for relieving stomach pain, as well as for the treatment of colds, improving blood circulation and reducing edema [55, 191].

Since ancient times in China, small galangal has been used by the people for the treatment of rheumatism, bronchial catarrh, ulcers, diabetes, for blood coagulation and for the treatment of throat infections [257, 259]. Currently, rhizomes are one of the most commonly used medications in TCM for the treatment of fungal vaginitis, and galangin is used as a dietary supplement [207].

Taste - Spicy. Properties (character) - warm. Correlation with channels: Spleen, Stomach [7, 8].

Functions and action. Dispersion of Cold to stop pain, warming up Zhong-jiao (Spleen and Stomach) to stop vomiting [7, 8]. According to other sources, the rhizome of Galangalus lesser expels Cold from Stomach, improves digestion, relieves pain, eliminates flatulence, has a pain reliever,anti-febrile, salivary, stomach tonic, appetite-increasing action [39].

Usage Information Available A. officinarum among the plants used in TCM to treathelminthiasis, as a means of stimulating the peristalsis of the stomach and intestines [34].

Indications. Cold pain in the abdomen from Cold in the Stomach. Vomiting due to Cold in Stomach [7, 8]. According to A.I. Schreter is prescribed for pain in the stomach (in the epigastric region) with a feeling of coldness, nausea, vomiting and sour regurgitation, which are caused by Cold in the Stomach [39].

Method of administration in TCM and doses. In decoctions on3–10 g, in the form of a powder - 3 g each [7, 8], according to other sources - 3–6 g of raw material per day [39].

The Brockhaus and Efron Encyclopedic Dictionary (1892) reports that in domestic medicine galanga belongs to intoxicants and is used for digestive disorders as an integral part of many drugs [12].

Seeds a. medicinal are recommended in oriental medicine for malaria, cholera, disorderstomach, heartburn, toothache [47], although in this case there may be confusion, since a. medicinal (small galangal [19]) use rhizomes, while in a. galanga (large galangal) - seeds [19]. "Big kalgan" (Javanese kalgan, in Indonesian - laos) in Indonesia has long been growing on about. Java ", has a large tuberous root, similar to the root of ginger, covered with a reddish-brown or creamy skin" [27].

According to the description of the Portuguese physician and naturalist Garcia de Orta (1501-1568), in Indonesia, the locals “those who came from Java (Java Indonesia), as well as midwives and local healers, do not sow the seeds of the Javanese galangal, but put them in salads. and they drink the infusion as a medicine ”[27].

The food and medicinal use of alpinia seeds is similar to that of all members of the Ginger family. Indicated for indigestion, pain in the stomach, nausea, vomiting, diarrhea due to the emptiness of the Yang. They are also prescribed for spermatorrhea, enuresis in children, salivation [3]. For a. holly, it is known that the seeds have a pungent (spicy) taste and a warm character [3, 35].

2. Application in homeopathy

Rhizome a. medicinal is used in homeopathy [1, 5, 6, 12, 16, 18, 21, 24, 39, 97, 117]. The plant is included in Appendix 2 to the order of the Ministry of Health of the Russian Federation dated November 29, 1995 No. 335 (as one of the positions in the nomenclature of domestic homeopathic medicines) [5, 6, 18, 21, 24], in the State Register of Medicines (2002) [14 , 18], the German Homeopathic Pharmacopoeia [21, 97, 117] and the Heel catalog [21, 116].

According to the German Homeopathic Pharmacopoeia GHP (2000) [97], the raw material is dried rhizomes A. officinarum (Galanga) containing at least 4 ml of essential oil in 1 kg of raw materials. In accordance with the requirements of GHP (2000), the raw material should not contain any admixture of rhizomesKaempferia galanga L., which differ in size (up to 4 cm thick) and light-colored central cylinder [97].

Matrix tincture is prepared from dried [1], according to other sources - from fresh crushed rhizomes

according to method 4a using 86% (by weight) ethanol [97]. The finished matrix tincture has a color from yellowish-brown to reddish-brown, the smell is aromatic, the taste is hot, scalding, aromatic [97].

Dilutions used: 3X, 3 and higher. The main indications are diarrhea, gastroenterocolitis [1].

3. Modern understanding of the biological action of Alpinia officinarum

Domestic researchers show practically no interest in either experimental or clinical research a. medicinal, which is apparently explained by the rare and mainly food use of these rhizomes in Russia. We have found domestic bibliographic sources containing information on the biological effect of the food use of this plant as a spice [1, 3, 19, 28–32] and on the use in traditional and folk medicine of different countries [1, 3, 4, 7, 25 , 39]. We have not identified the results of domestic experimental and clinical studies in the available literature. The publications are only of historical and informational and analytical nature in terms of food use and traditional medical use.

According to O.D. Barnaulova, “the rhizome of alpinia has a diaphoretic, diuretic, carminative effect; expels helminths, stimulates appetite, increases gastric secretion, bile secretion, and therefore is indicated for hyposecretory gastritis, cholecystitis, bile stasis (cholestasis), cholelithiasis, hepatitis, “animal bites” [3, 4]. Like other members of the Ginger family, small galangal exhibits anabolic, antitoxic, tonic, immunomodulatory effects [3].

Special attention of O.D. Barnaulov draws on the property of alpinia rhizomes to increase potency, erection, that is, to have a positive gonadotropic effect, "which should attract the attention of sexopathologists." According to him, galang "has a positive effect on stress resistance and reproductive functions of patients" [3]. Rhizomes also act carminatively, stimulate respiration [1].

Abroad, there is a noticeable interest in the study of a. medicinal is explained by ethnobotanical and ethnopharmacological data, confirming the use in traditional medicine of different countries and a wide range of its biological action, due to the rich complex of biologically active substances [20, 55].

Generalized views of the early XXI century on biological action a. medicinal products were presented by Duke JA (Table 1) in the Handbook of Medicinal Herbs [81] and in the CRC handbook of medicinal spices [83], as well as in the official Medical Directory of Herbal Medicines (PDR for Herbal Medicines) [147]. In these publications, attention is drawn to a significant number of references to medicinal properties that require confirmation from the standpoint of evidence-based medicine.

More recent studies indicate that the rhizome of a. medicinal (various extracts, as well as isolated groups of biologically active substances and individual compounds) exhibits a wide spectrum of pharmacotherapeutic actions, including anti-inflammatory, antibacterial, antioxidant, anti-osteoporotic, anti-obesity, antitumor, inhibitory enzymes, as well as unique antiviral properties [43, 55, 62, 87 , 193, 243] (Sections 3.14 and 4).

3.1. Biological activity of extracts and various extracts from rhizomes a. medicinal

In 2017, a group of researchers from Brunei (University of Brunei Darussalam) performed a review of experimental studies on the study of extracts and fractions of different polarities from different parts of the plant (leaves, roots, rhizomes, aerial parts). Extraction was carried out with various solvents (methanol, ethanol, ethyl acetate, hexane, dichloromethane, water, chloroform, petroleum ether) using adequate methods: maceration, percolation, ultrasonic extraction and in a Soxhlet apparatus, etc. - solvent ". Extracts, fractions, and individual isolated compounds were studied for their biological activity [55].

Fractionation and isolation of biologically active substances in combination with bioanalysis is by far the most widely used approach for evidence-based pharmacological studies. in vitro and in vivo, with where each extractant and the fraction isolated with its help are examined for their potential biological activity. The study of each of the isolated fractions can lead to the identification of new promising compounds for the creation of drugs.

Table 1

Biological activity and types of action (in alphabetical order) according to [81]

No.	Type of action	Evidence-based. base	No.	Type of action	Evidence-based base
1	Antibacterial	1; KOM; PH2	ten	Anti-inflammatory	2; KOM; PH2
2	Antidiuretic - promotes fluid retention in the body by participating in regulation of the amount of water, incl. by increasing reabsorption (increasing concentration of urine and reducing its volume)	f; DEP	eleven	Antineoplastic	1; PNC
3	Antiperiodic - preventative regular relapses	f; EFS	12	Antiulcer	1; PNC
4	Antiprostaglandin	2; KOM	13	Stimulating	1; EFS; MAD; MPI; PNC
5	Antispastic (antispasmodic)	2; KOM; PH2	fourteen	Stimulating salivation	f; EFS
6	Aperitif	f; PH2	15	Tonic	f; DEP; EFS
7	Aphrodisidic - acts as an aphrodisiac	f; DEP	16	Sedative	f; DEP
eight	Carminative	f; EFS; PNC	17	Emmenagic - pro waking menstruation major bleeding	f; MAD
nine	Gastric	f; EFS; MAD; MPI			

Note to table 1 and 4:
DAA - edition data [82], DEP - edition data [232], EFS - edition data [216], GMH - edition data [102], HHB - edition data [152], JLH - edition data [115], KOM - edition data [58], MAD - edition data [165], MPI - data from 2 editions [126, 127], PHR - plants whose efficacy has been confirmed by Commission E (KOM) and included in the 1st edition of the PDR for Herbal Medicines [93], PH2 - Commission E (KOM) approved plants included in the 2nd edition of the PDR for Herbal Medicines [104], PNC - data from the edition [239].

1 - Evaluation of effectiveness: the chemical in the plant or in the plant extract has been shown to be active: either it has been proven experimentally (in animals), or in vitro; but the evidence for clinical efficacynot yet available [81],

2 - Evaluation of efficacy: an aqueous extract, a decoction or tea from the plant, possibly also an ethanol extract, has shown activity, which has also been supported by proven efficacy in clinical trials. In most cases, effectiveness has been proven and approved by Commission E (KOM) and Tramil Commission (TRA) [81],

f - Evaluation of effectiveness: activity data available from traditional or traditional medicine; however, adequate scientific research has not yet been carried out [81].

According to [55], methanol is considered the most preferred extractant for obtaining primary crude recovery, which can be additionally fractionated using other solvents. It was also revealed that 100% methanol is the least toxic extraction solvent among other extractants (hexane, chloroform, dichloromethane, acetone and an aqueous solution) when testedin vitro on cell cultures [186]. Minimal toxicity when exposed to cell culturesin vitro is combined with a proven lack of influence of the solvent itself onantitumor activity of extracts [55].

The established types of action of extracts and fractions obtained using organic solvents and the method of re-extraction are presented in table. 2 (specific connections are discussed below in sections 3.2–3.14).

table 2

Types of action of various extractions
from leaves (L), grass (Tr), roots (K) and rhizomes (Ksh) a. medicinal (according to [55])

Part growing niya	Extraction method	Activities	Ex- exactly Nick
2.1. Methanol extracts containing flavonoids and diaryl heptanoids			
Ksh	Maceration	Anti-inflammatory, in vitro - antioxidant	118
Ksh	72-hour raw material soak in 99.8% methanol	Anticancer	98
L and Ksh	2-hour ultrasonic treatment with 100% methanol extraction	High antiproliferative activity leaf extract, comparable to rhizome extract	186
Ksh	Ultrasonic extraction	Antioxidant	66
TO	Extraction with 70% methanol at 80 ° C for 3 hours	Antioxidant	143
2.2. Ethyl acetate extracts from various rhizome extracts			
Ksh	Extraction with ethyl acetate from metal extract	Anti-inflammatory, antioxidant	118
	Extraction with ethyl acetate from acetone extract	Inhibiting nitric oxide production	170
		Anticancer, enzyme-inhibiting	
	Extraction with ethyl acetate from dried ethanol extract	Anticancer for various types of cancer, cytotoxic for various cell lines	154, 155
2.3. Chloroform extracts from various rhizome extracts			
L and Ksh	Ultrasonic extraction for 2 h	High antiproliferative activity	186
Ksh	Chloroform release from methanol extract	High antioxidant activity	162, 163
Ksh	Chloroform release from ethyl acetate extract	Anticancer activity	234
2.4. Ethanol extracts of various parts of a. medicinal			
Terrestrial part	Hot and cold maceration 50% ethanol	Antibacterial, antioxidant. Lack of antifungal	215, 256
-	Maceration with 95% ethanol at 70 ° C for 6 hours	Low antibacterial	197
Ksh	Soak in 40% ethanol within 2 hours	Antibacterial, enzyme-inhibiting	122
Ksh	Extraction in a Soxhlet apparatus	Anticancer	220
2.5. Hexane extracts of various parts of a. medicinal			
L and Ksh	Ultrasonic extraction	High antiproliferative activity rhizomes	186
Ksh	Extraction in a Soxhlet apparatus	Inhibition of nitric oxide production	196
2.6. Dichloromethane extracts of various parts a. medicinal			
Ksh	Extraction in a Soxhlet apparatus	High anti-cancer activity	129, 142
L and Ksh	Ultrasonic extraction	High antiproliferative activity both leaves and rhizomes	186

Numerous studies have also been conducted on aqueous extracts to mimic the traditional practice of drinking rhizome tea. A. officinarum. However, unlike methanol,aqueous extracts exhibited minimal biological activity without demonstrating antitumor, antiproliferative, and anti-inflammatory effects [55]. The differences in the spectrum of action and the severity of the effects are explained by the fact that the complex of BAS aqueous extracts may differ from BAS extracts obtained using other solvents, or such extracts may contain

similar compounds, but in different concentrations [55].

Results of studying water extracts a. medicinal products are consistent with previous studies for other plant species: extracts obtained using organic solvents show more stable scientific results in comparison with aqueous extracts from the same types of raw materials [189]. In addition, some water-soluble compounds, such as flavonoids and some other phenolic compounds, show selectivity or show no significant biological activity [182, 246].

Nevertheless, with some methods of aqueous-alcoholic extraction [76], pronounced antioxidant and anti-inflammatory activity was shown [197]. In particular, plant materials, which were extracted by shaking or boiling under reflux in water-alcohol mixtures, gave better performance with a higher content of polyphenolic compounds and more pronounced antioxidant activity, compared with the use of

100% aqueous or 100% alcoholic extractant [99, 122, 143, 146, 215, 221].

Aqueous extracts from methanol extracts of rhizomes showed significant antioxidant activity against the background of a very modest antiproliferative effect, in comparison with other extracts obtained using methanol, hexane, chloroform, dichloromethane, and acetone [186].

Traditional rhizome tea also did not show any significant antiproliferative activity against the AMoL THP-1 cell line within 24 hours. Similar results were obtained for aqueous extracts and on the COR L23 cell lines of non-small cell lung cancer and the MCF7 cell line of human breast adenocarcinoma when tested even at the highest concentration of 25 μg / ml and after 48 h of exposure [142].

The aqueous fraction of the acetone extract showed no anti-inflammatory effect (no inhibition of NO production on the LPS-induced macrophage cell line RAW 264.7 was recorded) [169], and also did not inhibit melanogenesis and proliferation in the 4A5 B16 melanoma cell line
[170].

Sections 3.2–3.14 describe specific experimentally proven effects for various extracts and biologically active substances from rhizomes a. medicinal.

3.2. Antineoplastic activity

Various biologically active substances in rhizome extracts A. officinarum obtained using 95% of ethanol and other organic solvents showed antiproliferative activity in the experiment, which causes an antitumor effect on numerous lines of cancer cells [49, 142, 223, 255].

Targeted experiments were carried out on standardized substances from the rhizomes of a. a drug group of researchers from Saudi Arabia and Egypt with the aim of confirming and objectifying antitumor activity [44]. To obtain the substance, the rhizomes were dried, ground into powder, and extracted with 95% ethanol by percolation until depletion for 2 days as described in [52]. Then it was filtered through a cotton filter and evaporated using a rotary evaporator at 25 ° C to the specified volume according to the method described in [53]. The chemical composition and quality indicators of the substance obtained by the researchers were described in detail by us earlier [20].

For studies on animals, the obtained alcoholic dry extract of rhizomes was dissolved in fresh distilled water using the emulsifier Tween 80 [85]. The experiment was carried out on Swiss albino mice of both sexes (35–38 g) purchased from the vivarium of the Alazahar University (Cairo, Egypt) [44]. The animals were kept in polypropylene cages under standard environmental conditions [187].

Experimental studies were carried out in vitro on 5 cell lines (Table 3): Hela (cervical cancer), CACO (colorectal cancer), Pc3 (prostate cancer), HCT-116 (colon cancer) and A-549 (lung cancer), as published [228] at the Regional Center for Mycology and Biotechnology, Al-Azhar University (Cairo, Egypt) [44].

The study made it possible to reveal a dose-dependent cytotoxic effect in comparison with the effect of vinblastine sulfate as a standard drug (Table 3).

Table 3

Results of studying the antitumor activity of ethanol extract of rhizomes a. medicinal (IC_{50}) on 5 cell lines [44]

Cell line	IC_{50}(μg / ml)	
	Extract	Vinblastine sulfate

Cell line	IC_{50}(μg / ml)	
	Extract	Vinblastine sulfate
A-549 (lung carcinoma)	6.72 ± 0.50	24.60 ± 0.70
CACO (intestinal carcinoma)	7.6 0 ± 0.30	30.30 ± 1.40
HCT-116 (colon cancer)	32.30 ± 3.10	3.50 ± 0.20
Hela (cervical cancer)	24.50 ± 1.10	59.70 ± 2.10
Pc3 (prostate cancer)	50.00 ± 2.40	21.20 ± 0.90

It was found that the maximum antitumor activity A. officinarum manifests itself in relation tocell line A-549 (lung carcinoma) and CACO (colorectal carcinoma). Accordingly, IC_{50} were 6.7 ± 0.5 and 7.6 ± 0.3 μg / ml, and this effect was even better than that of the standard preparation of vinblastine sulfate (24.6 ± 0.7 and 30.3 ± 1.4 μg / ml for A-549 and CACO, respectively). The rest of the results on three cell lines were assessed by the authors as promising, and IC_{50} extract a. drug was better on the Hela cell line (cervical cancer) than for vinblastine sulfate (24.5 ± 1.1 μg / ml and 59.7 ± 2.1 μg / ml, respectively). Minimal effect has been reported for Pc3 (prostate cancer) with IC_{50} for extract 50.0 ± 2.4 μg / ml versus IC_{50} 21.2 ± 0.9 μg / ml for vinblastine sulfate [44].

In this study, the antitumor effect was attributed to the action of phenolic compounds [44, 204]. It has previously been shown that the flavonoid galangin fromA. officinarum suppresses cellular invasion by suppressingepithelial-mesenchymal transition and inducing apoptosis in renal cell carcinoma [63].

Ethanol extracts obtained from dried rhizomes A. officinarum in the Soxhlet apparatus,showed the highest activity in MTT analysis (a colorimetric test for assessing the metabolic activity of cells) against the PC-3 prostate cancer cell line compared to extracts obtained using other solvents (petroleum ether, chloroform, water). At the same time, the ethanol extract demonstrated an effective decrease in the growth of cancer cells [220]. 80% aqueous acetone extract from rhizomesA. officinarum inhibited melanogenesis in stimulatedtheophyllin of murine melanoma B16 4A5 cells, and the flavonoid galangin was a representative component of this species of the genus alpinia, which induced apoptosis of BEL-7402 cells through the mitochondrial pathway [160, 170, 253].

In addition, among the components isolated from this extract, 4 diarylheptanoid (DAG) inhibited melanogenesis with IC $values_{50}$ (half of the maximum inhibitory concentration) in the range from 10 to 48 microns. Of these, 3 DAGs inhibited the expression of tyrosinase mRNA and tyrosinaselated proteins-1 and proteins-2, as well as the level of the protein associated with the microphthalmos of the transcription factor. In this case, DAGA. officinarum caused distinct but overlapping effects on the translatom B-lymphoblastoid cells [133].

According to experts, alpinia DAGs have a very interesting structure [20], which is reflected in biological activity: a chalcone or flavanone fragment attached to the diarylheptanoid skeleton has a pronounced antiproliferative effect against human fibrosarcoma HT-1080 and highly metastatic carcinoma of the mouse colon 26-L5 [95, 253]. The attachment of the chalcone part enhances the antiproliferative activity of DAG [46, 253].

Study of antiproliferative activity of hexane extracts of leaves and rhizomes A. officinarumBased on the analysis of MTS on the AMoL THP-1 cell line, it was shown that the leaf extract has a significantly higher antiproliferative activity at a concentration of 2 mg / ml, compared to rhizomes. However, when the leaf extract was diluted to a concentration of 0.1 mg / ml, its antiproliferative activity was sharply reduced [186]. In the same model, dichloromethane extracts of both leaves and rhizomes, including derivatives of hydroxycinnamic acids and β-sitosterol, showed a very significant antiproliferative activity with 100% cell death at concentrations of 0.1 and 2 mg / ml for 24 h [186].

Lee CC and Houghton P. (2005) studied the antitumor activity of the same dichloromethane extracts using sulforhodamine B. The investigated extracts showed the highest cytotoxicity against human non-small cell lung cancer cell line L23 COR for 48 h with an IC $value_{50}$ 5.4 ± 0.51 μM [142].

Individual compounds isolated from dichloromethane extracts: 1 ›-acetoxychavicol acetate (comp. No. 13.1. [20]), trans-pcoumaroyl diacetate (No. 13.2.), 4-hydroxycinnamaldehyde (No. 13.3.) And β-sitosterol (No. 13.4.) (Hereinafter, all compounds are numbered according to publication [20]) were also tested by Lee CC and Houghton P. (2005) for cytotoxic activity. Connection No. 13.1.

showed the highest activity at IC values$_{50}$ 5.8 ± 0.2 μM and 8.6 ± 0.0 μM, against the COR L23 cell lines and MCF7 human breast adenocarcinoma, respectively [142, 169].

When tested against the non-cancerous MCF5 cell line, compound # 13.1. showed a higher selectivity of cancer cells in relation to the COR L23 cell line compared to the MCF7 cell line, with a selectivity factor of 2.83 and 1.91, respectively, whereas compound No. 13.4. showed no cytotoxic activity against all tested cell lines [142, 169].

Some of the highlighted connections A. officinarum has even shown discriminatory tolerancein relation to normal cells, especially compound No. 13.1., isolated from dichloromethane extract of rhizomes A. officinarum [142], in which it was found that the 1'-acetoxyl group in the chavicol analogue significantly contributes to its cytotoxic activity [128, 179].

Basri AM et al. (2017) consider this message promising for the search for a safe treatment of cancer patients, since drugs approach the ideal if they are selective and targeted at a specific point of application, and also do not cause genetic and chromosomal aberrations that can lead to toxicity and unwanted side effects [55].

S. Ghil reported the ability of methanol extract of rhizomes A. officinarum inhibit proliferation of cells of the human breast cancer cell line MCF-7 depending on the dose and time, contributing to the arrest of the cell cycle, therefore, inducing cell apoptosis (Table 2) [98]. In another study, the antiproliferative activity of not only rhizomes, but also leaves was studied.A. officinarum. Methanol extracts (100% methanol) at a concentration of 2 mg / ml showed a significantly higher antiproliferative activity of the leaf extract compared to the rhizome extract against the AMoL THP-1 cell line [186].

To clarify the biologically active substances responsible for various mechanisms of antitumor action, in 2009.Matsuda H. et al. the ethyl acetate fraction was isolated from the crude acetone extract of rhizomes a.medicinal [170]. The purified fraction showed higher activity compared to extracts obtained using other solvents (acetone and aqueous solution).

Researchers considered several compounds to be responsible for the shown activity [170]: No. 1.5. (galangin), no. 1.9. (kaempferid), no. 5.1. (5-hydroxy-7- (4'-hydroxy-3'-methoxyphenyl) -1-phenylheptan-3-one), no. 5.2. (pinobaxin), No. 5.3. (5-hydroxy-1,7-diphenyl-3-heptanone), no. 5.4. (7- (4 "- hydroxy-3" - methoxyphenyl) -1-phenylhept-4-en-3-one), No. 5.5. (3,5-dihydroxy-1,7-diphenylheptane), no. 5.6. (3-phenylpropanoic acid) and No. 5.7. (zingeron) [20].

Of the listed BAS, only compounds 1.5., 5.4. and 5.5. ([20]) showed lipopolysaccharide (LPS) -induced inhibition of nitric oxide (NO) production in the RAW 264.7 mouse macrophage cell line. Connections No. 1.5., 1.9., 5.1., 5.3., 5.4. and 5.5. ([20]) significantly inhibited melanogenesis in theophylline-stimulated melanoma cells B16 4A5, a No. 1.5., 1.9. and 5.4. inhibited the enzymatic activity of fungal tyrosinase [170] (Table 2).

According to SN Omoregie et al. (2013), chloroform extracts of leaves and rhizomesA. officinarum showed a very high antiproliferative activity against the AMoL THP-1 cell line with 100% cell death at concentrations of 0.1 and 2 mg / ml for 24 hours [186]. Later, from the rhizomes a. medicinal was isolated and thoroughly studied [181, 234] alpinisin A (No. 7.6. [20]) - adduct of DAG-sesquiterpene nature).

Connection No. 7.6. ([20]) has been tested for cytotoxic activityin vitro versus severalhuman tumor cell lines: gastric carcinoma - 7901 (SGC-7901), human breast cancer - Michigan Cancer Foundation - 7 (MCF-7) and Caski Carcinoma Caski cell lines. Revealed antitumor activity and pronounced inhibitory effects with IC $_{50}$, respectively 11.42, 15.14 and 14.78 μM [181, 186]. In addition to cytotoxic properties and tumor growth regression, some biologically active substances a. drug demonstrated a pronounced antimetastatic potential. In particular, cardamonin, galangin and flavocavin B isolated fromA. officinarum (as well as from A. katsumadai and A. pricei), showedantimetastatic properties in Lewis lung carcinoma, fibrosarcoma, melanoma, renal carcinoma and in relation to cell carcinoma of the breast [193].

In general, as noted by the authors of the review [199] devoted to the antitumor properties of A. officinarum,the anti-cancer potential of this plant is of great interest from the scientific community. Every year there is more and more evidence that the plant contains powerful antiproliferative agents, which may serve as the basis for the most modern anticancer drugs in the near future [199]. Studying the mechanisms of action of biologically active substances can help to prevent possible adverse effects, therefore, to maximize their effectiveness [55].

3.3. Antibacterial and antifungal action

Ethanol extract of rhizomes A. officinarum (maceration 40% ethanol for 2 hours) inhibited

reaction of bacterial fatty acid synthetase, β-ketoacyl-ACP reductase (FabG). It has also shown effective inhibition of the proliferation of gram-positive bacterial strains:S. aureus, αhemolytic streptococcus, β hemolytic streptococcus and Streptococcus pneumoniae [122].

IB Abubakar et al. (2018) described the bifunctional role of DAGs in terms of their antibacterial and anti-inflammatory activity. In particular, with reference to (Subramanian et al., 2009), it was shown on human peripheral blood mononuclear cells that DAGs exhibit antibacterial activity and suppress inflammation induced by enteropathogenic lipopolysaccharides.E. coli (Escherichia coli) [43].

In addition, it was found that 3 alpinia DAGs: trans, trans-1,7-diphenylhepta-4, 6-dien-3-one, (5R) -trans-1,7-diphenyl-5-hydroxyhept-6-en3-one and (3S, 5S) -trans-1,7-diphenylhept-1-ene-3,5-diol exhibit pronounced antimycobacterial activity in terms of the accumulation and release of EtBr, as well as a synergistic effect with rifampicin, which should be taken into account when screening lipophilic plant extracts showing antimycobacterial activity [103].

During phytochemical screening of biologically active substances, potentiating the action of antibiotics, from rhizomes A. officinarum was isolated as an individual diterpene of antimicrobial action [110]. It has also been shown that its antifungal activity is associated with a change in the membrane permeability resulting from the alternation of membrane lipids [110].

In general, the antibacterial and antifungal effects of a very wide spectrum are described in sufficient detail for both terpenoid and phenolic complexes of rhizomes. A. officinarum (sec. 3.14).

3.4. Anti-inflammatory action

The carrageenan paw edema test is used to screen for anti-inflammatory drugs because it involves inhibition of the release and / or action of several neurotransmitters, histamine, serotonin, kinin, and prostaglandin [78, 171]. Dried rhizome extractA. officinarum(maceration in methanol) demonstrated inhibition of edema of the right hind paw in carrageenan-induced inflammation in rats (Table 2) [118].

A purified ethyl acetate extract from a methanol extract containing the flavonoid galangin and DAG 5-hydroxy-7- (4 ›-hydroxy-3› -methoxyphenyl) -1-phenylheptan-3-one showed high efficiency in an acute inflammatory animal model comparable to nonsteroidal anti-inflammatory drug diclofenac, used in the experiment as a control [118]. The aqueous extract obtained in an autoclave with deionized water also had anti-inflammatory activity, moreover, it was more pronounced in comparison with the ethanol extract.A. officinarum [197]. Anti-inflammatory effect of ethanol extract a. medicinal likein vitro and in vivo is also shown in [66, 112, 215].

3.5. Inhibition of nitric oxide (NO) production

Study of the anti-inflammatory activity of the hexane extract of rhizomes A. officinarum andDAG isolated from it (comp. 1.18. - [20]) revealed inhibition of nitric oxide (NO) production in LPS-induced macrophage cell line RAW 264.7, which was mediated by inhibition of the transcriptional activity of nuclear factor-kβ, a gene regulator involved in cell proliferation, cellular adhesion and inflammatory reactions [196]. Normally, nitric oxide regulates many intra- and intercellular processes and affects the cardiovascular system, gastrointestinal tract (GIT), urogenital, nervous and respiratory systems [33].

Nervous system. In the brainNO performs the function of a secondary messenger in the processes of intracellular signaling, as a neurotransmitter it participates in intercellular signaling, functionally connecting postsynaptic and presynaptic neurons [33]. The highest activity of NO synthase was found in the cerebellum, while the lowest activity was found in the hypothalamus, midbrain, striatum, cortex, hippocampus, and medulla oblongata. Along the efferent nerves, this agent regulates the activity of the digestive tract, respiratory and genitourinary systems. It is believed that nitric oxide is involved in the pathogenesis of Parkinson's disease, since its level in the brain increases in this pathology [175].

Genitourinary system. The level of nitric oxide in the blood of patients with Berger's disease (a varietychronic glomerulonephritis) significantly increases after the introduction of isosorbide-5-mononitrate. At the same time, proteinuria and filtration are significantly reduced in comparison with the basal level [203]. The participation of nitric oxide in the formation of interstitial cystitis has been shown [136].

Respiratory system. The protective and damaging effects of periodic hypoxia andthe role of nitric oxide in acute and chronic lung diseases associated with pulmonary hypertension [23]. Particular attention is paid to NO in bronchial asthma [203]. The effect of growth hormone on the level of nitric oxide and fibrosis of cysts in the lung tissue has been studied [101].

Oncology. NO is a precursor of carcinogenic N-nitroso compounds, at the same time

participates together with growth-stimulating factors, tyrosine kinase, Na^+/ H^+-exchanger, secondary messengers (cAMP, cGMP, inositol1,4,5-triphosphate, diacylglycerol, arachidonic acid and cyclic ADP-ribose) in Ca regulation^{2+}-mobilizing system of intracellular signal transmission and in the processes of cell division [33]. In addition, NO is released from compounds with antitumor activity, for example, nitrofurans and nitroimidazoles [10, 40].

NO increases the radiosensitivity of tumor tissues, since carbon radicals formed under the action of ionizing radiation on DNA in the absence of NO react with hydrogen atoms of neighboring proteins, which facilitates DNA repair [9].

Ethyl acetate extract from methanol extract of rhizomes a. medicinal containing the flavonoid galangin and 2 DAGs: 7- (4 ›› - hydroxy-3 ›› - methoxyphenyl) -1-phenylhept-4-en-3-one and 3,5-dihydroxy-1,7-diphenylheptane in experiment showed inhibition of nitric oxide (NO) production in the RAW 264.7 mouse macrophage cell line induced by lipopolysaccharide (LPS) [170].

The influence of NO on the course of the pathological process was also studied when determining the antioxidant, antiulcer and some other types of action of a. medicinal (Sections 3.9, 3.14.1).

3.6. Antioxidant action

Normal metabolism in the body, consumption and use of oxygen, for example, during respiration, cell growth and certain cellular immune processes, constantly generate also active oxygen species (ROS) - superoxide radical anion (O_2^-), hydrogen peroxide (H_2O_2), hydroxyl radical (OH) et al. [237]. If ROS are not effectively removed, then various pathological processes develop [110]. Oxidative stress is increasingly considered as an important risk factor for neurodegenerative [66] (Section 3.7) and many age-related diseases, including, in particular, osteoporosis [188] (excessive accumulation of ROS cannot be effectively eliminated by the antioxidant defense system, which contributes to oxidative stress and resulting in bone loss [194]) (Section 3.8).

The ability to reduce 2,2-diphenyl-1-picrylhydrazyl (DPPH) radicals is determined by the decrease in their absorption at 517 nm caused by antioxidants [56]. Many antioxidants that react quickly with peroxyl radicals may react slowly or may even be inert to DPPH [96].

According to [118], the extract of dried rhizomes A. officinarum (maceration in methanol) showeda promising dose-dependent effect of DPPH on free radical scavenging up to a concentration of 100 μg / ml (Table 2). Root extractA. officinarum (maceration 70% methanol at 80 ° C for 3 h), showed a pronounced dose-dependent antioxidant DPPH effect and significantly inhibited lipid peroxidation in treated H_2O_2 cells V79-4 [143]. Methanol extract of dried rhizomesA. officinarum obtained by ultrasonic extraction also showed goodantioxidant DPPH activity [66] (Table 2).

Extract A. officinarum was one of the 5 plant methanol extracts studied at the Biotechnology Research Institute of Hongquang University (Taiwan) in 2011 for the presence of antioxidant effects. In comparison with four other objects of study, the dominant fraction in the extract of alpinia rhizomes was the triterpenoid fraction, while the phenolic fraction in the hawthorn fruits, the flavonoid fraction in the spatolobus shoots, and tannins in the uncaria [66]. The total content of phenols in 1 g of the studied extract of rhizomes a. drug was 376.8 ± 5.5 mg (in terms of gallic acid), flavonoids - 659.5 ± 10.4 mg (in terms of quercetin), triterpenoids - 109.8 ± 5.6 mg (in terms of ursolic acid), tannins - 45.4 ± 1.2% [66].

All 5 studied extracts showed a pronounced ability to absorb ROS (chemiluminescence method: HRP-luminol-H_2O_2 can significantly enhance light radiation), and their antioxidant activity was higher than that of L-ascorbic acid and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid [66]. According to the authors of the study, it was the high total content of triterpenoids that determined the good antioxidant activity of the a. medicinal in tests pyrogallol-luminol and $CuSO_4$-Phen-Vc-H_2O_2 [66]. At the same time, according to [55], the antioxidant effectA. officinarum can be caused not only by triterpenoids, but also by a number of othersconnections. In particular, flavonoids and other polyphenols of alpinia possess the ability to absorb ROS [192]. In support of this, purified ethyl acetate extraction from methanol extract (maceration in methanol) containing the flavonoid galangin and DAG 5-hydroxy-7- (4 ›-hydroxy-3› - methoxyphenyl) -1-phenylheptan-3-one showed high antioxidant activityin vitro [118].

Study of the antioxidant activity of chloroform extracts from methanol extract of rhizomes a. drug was carried out by autoxidation of methyl linoleate [162, 163]. The highest antioxidant activity was shown by g-Pcumaryl alcohol methyl ether. The rest of the connections of this

fractions (Nos. 7.2. –7.5. [20]) showed an antioxidant activity lower than that of αtocopherol as a reference antioxidant standard [55]. The same method was used to study the antioxidant activity of the extraction obtained by re-extraction with water from the methanol extraction (phenol alcohols). Isolated from the water fraction ncoumaril alcohol showed higher activity compared to 1,5 bis(4-hydroxyphenyl) -2-(hydroxymethyl) -4-penten-1-ol contained in the same fraction [162, 163]. The aqueous extract obtained in an autoclave with deionized water also had a more significant activity compared to the ethanol extract.A. officinarum [197].

Antioxidant effect of ethanol extract a. medicinalin vitro and in vivo also shown inworks [66, 112, 215]. Thus, the antioxidant effect of rhizome extracts a. medicinal products obtained using various solvents are considered fully proven [55].

3.7. Neuroprotective (neuroprotective) action

Surplus production of ROS (•O_2^-, •OH, H_2O_2) generated including during normal exchange substances in the body, oxygen consumption during respiration, in some cellular immune functions [66], lipid autooxidation [51, 65] and other processes, according to modern concepts, is associated not only with aging and with many diseases, including atherosclerosis, cancer, inflammatory diseases but also with some neurodegenerative diseases [65, 109]. Since the main mechanism of development of the latter is currently considered damage by free radicals [65, 66], the results of studies of antioxidant and neuroprotective effects often correlate. In this case, rat pheochromocytoma cells (PC12, CRL-1721) are chosen as a model for the study of neurodegenerative diseases [66].

Previously, it was shown that, for example, methyl gallate is able to significantly uptake ROS and weaken the apoptotic response resulting from prolonged oxidative stress during apoptosis of PC12 cells induced by H_2O_2 [69]. Sesaminol glucosides have a protective effect on amyloid beta$_{25–35}$ for (Aβ$_{25–35}$) -induced death of PC12 cells, and their effect may be related to the effect of trapping ROS in the study of Alzheimer's disease [141]. Aqueous extract of hooksUncaria rhynchophylla alsosignificantly reduces the formation of ROS and the death of PC12 cells induced by 6-hydroxydopamine, which was used to study Parkinson's disease [208]. The same cell line and model (apoptosis of PC12 cells caused by H_2O_2) were successfully used to study the protective neuroprotective effect of puerarin in neurodegenerative diseases [131].

Summarizing the results obtained, Chang CL and Lin CS (2012) concluded that compounds exhibiting neuroprotective activity in toxicity induced by H_2O_2 in relation to PC12 cells, are reliably potential candidates for the treatment of neurodegenerative diseases (after a thorough study of the mechanisms of their action in vivo) [65]. Therefore, having established in 2011 the presence of an antioxidant effect in 5 plant methanol extracts (Section 3.6.), CL Chang et al. (2012) used the PC12 cell line as a model to study the induced neurogrowth and neuroprotective effect of these extracts on H_2O_2-induced death of PC12 cells [66].

One of the 5 mentioned subjects of study of neuroprotective effect on PC12 cells was the extract A. officinarum (along with Spatholobus suberectus, Uncaria rhynchophylla, Drynaria fortuneiand Crataegus pinnatifida) [66]. Atin vitro exposure H_2O_2 (40 μM, 12 h) on the model "Inhibition of H_2O_2- induced cell death PC12 ", the cell viability decreased to 59.0 ± 5.1%, but against the background of the use of the investigated extracts at a concentration of 0.5-5.0 μg / ml, protecting cells from H_2O_2, stimulation of neurogrowth activity was observed, that is, the viability of PC12 cells increased in comparison with the control. However, the neuroprotective effect of the extractsA. officinarum and Drynaria fortuneiturned out to be very moderate in this experiment in comparison with the other three samples [66].

After 4 years, Huang et al. (2015) reported that DAG fromA. officinarum 7- (4-hydroxyphenyl) -1-phenyl-4Ehepten-3-one has a pronounced effect on neuronal differentiation and neurite growth in vitro and in vivo [225]. A year later, Huang et al. (2016) demonstrated the neuroprotective effect of DAG (4E) -7- (4-hydroxyphenyl) -1-phenylhept-4-en-3-one from a. drug against toxicity caused by β amyloid, on neuronal cells. BAmyloid is considered one of the main causes of diseaseAlzheimer's (the most common neurodegenerative disorder characterized by progressive cognitive impairment) [121].

As a result of the studies carried out, it was shown that the studied DAG has a neuroprotective effect in neurotoxicity caused by βamyloid. When damaged by β-amyloid oligomers, the dendrites of neurons became atrophic and simplified; however, such disorderssignificantly stopped after treatment with the DAG substance. Moreover, under the influence of this substance, the levels of apoptosis and oxidative stress caused by βamyloid. Further analysis showedthat the anticaspase and dendritic protective effects of DAH depend on the activation of the PI3K-mTOR pathways

(phosphatidylinositol-3-kinase (PI3K) - mammalian target of rapamycin (mTOR)). The results obtained allowed the authors of the study to characterize (4E) -7- (4-hydroxyphenyl) -1-phenylhept-4-en-3-one as a promising compound with neuroprotective action in damage to the integrity of dendrites β amyloid and to increase cell survival in Alzheimer's disease [121].

After 2 years, Hui Liu et al. (2018) isolated from the rhizomes of a. medicinal range of DAG and DAG adducts with terpenes. In particular, two pairs of new enantiomers of diarylheptanoid-monoterpene adducts were isolated: (±) -alpininoids A and B, as well as three pairs of new enantiomers of diarylheptanoid-sesquiterpene adducts: (±) -alpininoids CE, along with four known diarylminoids R -5-hydroxy-1,7-diphenyl-3-heptanone, 1-phenyl-7- (4-hydroxy-3-methoxyphenyl) -4E-en-3-heptanone, 1-phenyl-7 (4-hydroxyphenyl) - 4E-en-3-heptanone and 1,7-diphenyl-4E-en-3-heptanone [157]. A detailed characterization of these compounds was presented by us earlier [20].

All isolated biologically active substances were tested for their neuroprotective activity against MPP^+ - induced damage to cortical neurons. It was shown that after exposure to 500 μM MPP^+ within 20 h, the viability of cortical neuron cells decreased to 62%. The dextrorotatory enantiomer of (+) alpinidinoid A (16 μM) significantly restored cell viability. At the same time, its (-) enantiomer did not show any neuroprotective effect, which, according to researchers, confirms the stereospecificity of the described neuroprotective activity [157].

The putative biosynthetic precursors of both enantiomers of alpinidinoid A (1-phenyl-7- (4-hydroxy-3-methoxyphenyl) -4E-en-3-heptanone and βmyrcene) were also evaluated for their neuroprotectiveanti-MPP activity$^+$-induced damage to cortical neurons, however, none of them showed a noticeable neuroprotective effect at the tested concentrations. This allowed the researchers to conclude that the hybridization of diarylheptanoid and monoterpene may be important for neuroprotective activity [157].

In 2020, Hui Liu et al. published the most recent results of studying the neuroprotective activity of dimeric DAH rhizomesA. officinarum [156]. At the first stage of the study, two new dimeric DAGs with two unusual binding patterns (alpinidinoids A (±) and B) and a new dimer of DAGs with a rare pyridine ring bond (alpinidinoid C) were isolated from the rhizomes. Then, by extensive spectroscopic methods and theoretical calculations, the structures of all compounds, including their absolute configurations, were determined [156] (their characteristics are presented in [20]).

When studying neuroprotective activity against oxygen-glucose deprivation and reoxygenation (OGD / R) damage in primary cortical neurons, it was found that the dextrorotatory enantiomer of alpinidinoid A (+) significantly improved OGD / R-induced apoptosis of neurons, which depended on activation of the AKT / mTOR signaling pathway. ... Therefore, the compound can be considered very promising for further clinical studies with the aim of creating modern natural neuroprotectors [156]. Antiamnesic effect of ethanol extract a. drug in Aβ-induced neurodegeneration in mice, due to antioxidant properties, was shown in [112].

Thus, to date, the neuroprotective properties of a. medicinal can be considered proven [75].

3.8. Anti-osteoporotic action

With the aging of the world's population, osteoporosis has already become a major global health problem. Osteoporosis is a progressive systemic disease characterized by low bone mineral density and deterioration of bone microarchitecture, which leads to an increased risk of fractures [94]. Long-term use of certain drugs (including estrogen, bisphosphonates and parathyroid hormone) to reduce bone loss in osteoporosis causes many adverse reactions, in particular an increased risk of endometrial and ovarian cancer [74, 217], atypical fractures of the femur [190], osteonecrosis of the jaw [168], venous thromboembolism [67], disorders of the nervous system [202].

Herbal medicine has been used as an alternative with promising efficacy and fewer unwanted side effects to prevent or reverse postmenopausal osteoporosis [218]. Herbal substances potentially have fewer side effects and have multiple pharmacotherapeutic effects on bones, making them more suitable for long-term or permanent use [148, 177].

A number of LR, for example, Epimedium (mountain woman) [244], Rhizoma drynariae [105] and Salvia miltiorrhiza [71], or biologically active substances such as icariin [89], resveratrol [84], show a preventive effect on bone loss caused by estrogen deficiency, inflammation, or physical inactivity. Herbal substances are economical, have a minimum number of side effects and are aimed at several

signaling pathways involved in bone metabolism [71, 84, 89, 105, 244].

A growing number of studies confirm that the main cause of bone loss after menopause and age-related bone loss is oxidative stress [90, 219], suppressing osteoblast differentiation, decreasing osteoblast lifespan, and increasing bone resorption by increasing the development and activity of osteoclasts [90, 219] 119], which leads to a shift towards the absorption of bone tissue to a greater extent than the formation of bone, i. E. to osteoporosis [119, 120].

Today it is considered proven that antioxidants are effective (and therefore necessary) for the treatment of osteoporosis [218]: they increase bone formation and / or suppress bone resorption [135, 183].

In 2015, a study was conducted at the Guangdong Medical University (GMU) to study the anti-osteoporotic effects of a. drug on the model of oophorectomy (OVX) in rats, as well as the effect of various fractions isolated from alpinia rhizomes on the activity of primary osteoblasts [218]. The choice of the object of research is explained by the fact that 1) antioxidants have a protective effect on the development of osteoporosis [167] (Section 3.6), 2) the effectiveness of flavonoids a. medicinal in relation to osteoblasts and suppression of osteoclast function [123, 206] is similar to the extract of Horny Goat Weed [218]. Moreover, about the effectiveness of a. medicinal as an anti-inflammatory agent for the treatment of diseases of the musculoskeletal system, including rheumatism, has been known for 2500 years in TCM and Ayurvedic medicine [54, 218, 226].

The extract for the study was obtained by boiling the rhizomes of a. drug under reflux in 98% ethanol, followed by purification by stripping and TLC (with the isolation of fractions F_1–F_5containing different amounts of flavonoids; galangin content was determined by HPLC method). In researchin vivo 36 female rats SpragueDawley aged 4 months (weighing 265 ± 14 g) was divided into 3 groups of 8 individuals: 1) OVX, 2) OVX with epimedium flavonoids (horny goat goose) (150 mg / kg / day), 3) OVX with alpinia extract (300 mg / kg / day); the remaining animals with imitation oophorectomy were used as a comparison group. The substances were administered orally daily, starting on the 3rd day after OVX, for 12 weeks. In researchin vitro primary osteoblasts were incubated with purifiedextract, galangin and F fractions$_1$–F_5 with or without hydrogen peroxide [218].

The control of efficacy and the volume of studies corresponded to the requirements of the "Guidelines for the care and use of laboratory animals of the National Committee of Science and Technology of China" (The study protocol was approved by the Expert Council on the Use and Care of Animals of the State Medical University (Zhanjiang, China) [218].

It was revealed that the introduction of alpinia extract significantly weakened osteopenia, accompanied by a decrease in the perimeter of osteoclasts (in percent) and the rate of bone formation per unit of bone surface, increased bone strength and prevented the deterioration of the microarchitecture of trabeculae associated with a decrease in the biochemical parameters of oxidative stress. In addition, treatment with extract, galangin, and isolated fractions (F_3, F_4) increased the viability, differentiation and mineralization of cells in osteoblasts (with H_2O_2 or without it) and eliminated the negative impact of H_2O_2 on cell apoptosis and the level of intracellular ROS. The effect on osteoblast formation was significantly correlated with the amount of flavonoids in the extract [218].

The effectiveness of the extract in terms of increasing the mass of bone tissue was evidenced by the results of histological and biochemical studies (for example, in OVX rats, a clear decrease in the level of the SOD enzyme was revealed [180]), as well as a significant increase in BMD (bone mineral density), BV / TV (relative bone volume) and Tb.Th (trabecular thickness), with a clear decrease (%) in Tb.Sp (trabecular separation), Oc.N (number of osteoclasts), Oc.Pm (perimeter osteoclasts) and BFR / BS of the tibia. Three-point bending tests on the femoral shaft have shown that the extract prevents a decrease in the degree of bending in OVX rats and improves the biomechanical properties of the bone. That is, the results of bone histomorphometry demonstrated that treatment with alpinia extract can partially prevent osteopenia and reduce the manifestations of bone destruction,

In research in vivo [218] also found that H_2O_2 can provoke an increase in the formation of ROS and subsequently lead to a decrease in the viability, differentiation, mineralization and apoptosis of cells, which is consistent with previous studies [146, 247]. In experimentin vitro [218] alpinia extract and fraction F_3 and F_4 neutralized the inhibitory effect of H_2O_2-induced oxidative stress on apoptosis, differentiation, mineralization and ROS formation of osteoblasts. These results strongly support the view that AOH can trap ROS and subsequently reduce oxidative stress.in vitro and in vivo [218].

Thus, the study performed for the first time revealed the beneficial effect of alpinia extract in osteopenia in operated (OVX) rats, as well as five fractions (F_{1-5}) alpinia, containing different amounts of flavonoids (including galangin), for differentiation and antioxidant activity in

osteoblasts in vitro. In particular, it has been reliably shown:
1) treatment with alpinia extract partially prevented bone loss, significantly improved bone microarchitecture, bone strength, and oxidative stress status in rats with OVX-induced osteoporosis; 2) the extract was more effective than Horny Goat Weed flavonoids in osteopenia associated with a decrease in the surface of osteclasts and the rate of bone turnover in OVX rats; 3) extract, fraction F_3, F_4 and galangin neutralized the harmful effects of oxidative stress on osteoblast differentiation (while other fractions did not affect the stimulation of osteoblast differentiation) [218]. Although the protective effect in OVX rats and osteoblast differentiationin vitrocorrelated with the galangin content in substances, the authors of the study obtained evidence that the anti-osteoporotic effects of alpinia are associated not only with flavonoids, but also with DAH and terpenoids (essential oil) [218].

Thus, it was found that ethanol extract a. medicinal, like its flavonoid fractions, significantly reduces bone loss, including by increasing bone formation and suppressing bone resorption associated with antioxidant effects [218]. The results of clinical studies have shown that the extract has a statistically significant effect on the reduction of symptoms of osteoarthritis of the knee joint with a good safety profile and minimal side effects from the gastrointestinal tract [48]. This allows the extract to be read. a promising drug for the prevention and treatment of osteoporosis and indicates the possibility of its safe wide clinical use [218].

3.9. Antiulcer activity

As a starting study for the study of antiulcer activity, a group of Chinese pharmacologists accepted the work [231], which revealed the effectiveness of oil extraction from the rhizomes of a. medicinal for hyperacid gastritis. ICR mice were randomly divided into 7 groups: control, model, Omeprazole group (0.014 g / kg^{-1}), Liangfu Group (tablets, 2 g / kg^{-1}), high dosage group a. medicinal, medium dose group a. medicinal, low dose group a. medicinal (respectively, 8, 4 or 2 ml / kg^{-1}). After 6 days of treatment, the mice were given reserpine. After that, gastric juice was collected from all mice (in each group), its volume, total acidity and pepsin activity were measured; in the serum of mice, the content of nitric oxide (NO), the activity of superoxide dismutase (SOD) and malondialdehyde (MDA) were determined [231].

It was shown that in the experimental groups of animals (with the exception of the group with a low dosage of A. medicinal) the activity of pepsin was inhibited, the volume of gastric juice and total acidity were reduced in comparison with the model group. In addition, the NO content increased, the SOD activity increased, and the MDA content decreased [231]. Thus, the authors of the study [231] considered proven the effectiveness of the oil extract for suppressing acidity, increasing the antioxidant response and activating protective factors in the treatment of hyperacid gastritis.

In 2015, Wei et al. showed that the extractA. officinarum exhibits antiulcer effect on the modelrats with ethanol-induced gastric injuries [233]; however, the mechanisms of action of the extract A. officinarum in the treatment of gastric diseases caused by NSAIDs was still unknown.Therefore, in 2018, Gong J. et al. studied the antiulcer activity of ethanol extract of rhizomesA. officinarum in a rat model of indomethacin-induced gastric injury. Indomethacin (0.3 g / kg) was orally administered to Sprague-Dawley rats to induce gastric damage. After 7 hours, the animals were injected with 0.03, 0.09, or 0.18 g / kg of LR extract, galangin (0.2 g / kg) or bismuth-potassium citrate (0.08 g / kg) once a day for 6 days. Control rats received an equivalent volume of pure extractant solution for 6 days. The lesion of the stomach was assessed by macroscopic ulcer and histological parameters. Cyclooxygenase and proteins of the non-cyclooxygenase pathway were quantified by Western blotting and ELISA [100].

It has been shown that the extract A. officinarum reduced gastric damage in a dose-dependent manner.The best results were demonstrated by a dose of 0.18 g / kg: a decrease in a large ulcer (from 20.23 ± 1.38 to 1.66 ± 0.37) and histologically (from 4.67 ± 1.03 to 0.33 ± 0, 51), a decrease in the level of TNF-α in serum (by 14.17%), an increase in the level of VEGF in the serum (by 1.58 times), an increase in the level of cyclooxygenase-1 (by 1.25 times, $p < 0.001$) in the mucous membrane stomach against the background of reversal of indomethacin-induced changes in the expression of proteins of the non-cyclooxygenase pathway ($p < 0.05$). Pure substance of galangin flavonoid, isolated from A. medicinal, was less effective as an antiulcer than the extract, indicating the contribution of several components of the extract to the protective effect. VS Honmore et al.

Thus, Gong J. et al. (2018) showed that rhizome extractA. officinarum and galangin

have antiulcer effect through cyclooxygenase and non-cyclooxygenase pathways. This can serve as an experimental confirmation of the long-term traditional use of small galangal (Section 1), and subsequently galangin for the treatment of gastric injuries [100].

The importance of the results obtained is due to the constant increase in the frequency of gastric injuries due to the widespread use of non-steroidal anti-inflammatory drugs (NSAIDs). According to Wolfe et al. (1999), mortality associated with gastric ulcer and other gastric damage caused by NSAIDs increases by 0.22% annually [240].

The current view is that NSAIDs such as indomethacin cause gastric damage, mainly because they block cyclooxygenase (COX) -1 and COX-2 [213]. NSAIDs selective for COX-2 or combination drug therapy may reduce these gastric side effects. However, selective inhibition of COX-2 does not eliminate the risk of gastroduodenal ulcers and their complications [140]. In addition, this approach is of little use for patients with a high sensitivity to NSAID-induced gastric damage [114, 139, 166] against the background of comparable (or even worse) toxicity to the kidneys and cardiovascular system [42]. The antiulcer activity of galangin is described in detail in Sec. 3.14.1.

Concomitant use of a number of mucosal protective drugs (eg, misoprostol), H2 receptor antagonists (eg, ranitidine), or proton pump inhibitors (eg, omeprazole) can reduce damage to the stomach or intestines to a limited extent. However, according to experts, further studies are needed to prove their real effectiveness from the standpoint of evidence-based medicine [114].

At the same time, based on the results of their own research, the authors of [100] consider it reasonable and expedient to include a. medicinal in the group of effective non-steroidal anti-inflammatory drugs.

3.10. Antihyperlipidemic activity

Adding rhizomes to the diet (high in fat) completely prevented enlargement of the liver, kidneys and spleen of hamsters, as well as an increase in serum TC, TGs, LDL-C and LDL-C / HDL-C. The activity of antioxidant enzymes also increased [207]. Ethanol extract of rhizomes reduced body weight gain and decreased TC, TGs, LDL-C levels, and leptin in rats fed a high-fat diet. HDL-C and HDL-C / TC ratio in the experiment also improved significantly [207].

According to [151], the antihyperlipidemic activity of rhizomes A. officinarum is due to the actiona whole complex of biologically active substances: curcumin, polyphenols, phytosterols and dietary fiber.

3.11. Immunotropic action

According to Chinese researchers, drugs and traditional remedies from the rhizome of a. medicinal have an immunotropic effect: “new studies have revealed an immunostimulating effect in allergies, especially in allergic rhinitis” [47]. However, we could not find reliable experimental or clinical confirmation in the available literature.

3.12. Antiviral properties

To date, there are reliable data that make it possible to state the pronounced antiviral properties of a. medicinal [62, 75], mainly due to DAH [157, 174].

According to experts, the unique antiviral properties of a. medicinal can be regarded as extremely promising in terms of creating modern drugs in connection with the emergence of virulent respiratory diseases not only in Asia and the Middle East [193].

3.13. Repellent activity and contact toxicity to insects

Rhizomes A. officinarum exhibit pronounced repellent and contact toxicity againstinsects, in particular Lasioderma serricorne - tobacco beetle [161]. This pest is considered worldwide one of the most harmful for foodstuffs exposed to storage - flour, dried fruits (especially raisins and dates), cocoa, cereals, herbs, spices, nuts, dry pet food, tobacco, etc. [41]. In general, direct and indirect losses of grain and grain-based products caused by pests in stored products vary from about 10% in temperate latitudes to almost 50% in humid tropical regions [238].

When setting up the experiment, the researchers used ethnobotanical data on the traditional centuries-old use of a. medicinal, like other aromatic plants, for

crop protection during storage, or for the so-called antagonistic storage [79, 153, 248], which is of practical value, including for home storage.

It has been shown that diethyl extract of rhizomes A. officinarum demonstrates a pronounced dose-dependentrepellent activity against tobacco beetle, reaching 91.3% at a dose of 0.20 μl / cm_2 within 48 hours after exposure. Contact toxicity against the same pest was also dose-dependent and reached more than 80% at a dose of 0.16 μL / cm_2 after 48 hours of exposure. LD $value_{50}$ for extract a. drug was 0.05 μl / cm_2 with a confidence interval of 95% from 0.02 to 0.08 μl / cm_2 after 48 h of exposure [161]. Similar activity of supercritical CO_2-extract from rhizomes is indicated for the red flour beetle Tribolium castaneum (Herbst), which poses a significant threat to stored food [243], as well as essential oil A. officinarum against many more pests: Sitophilus zeamais, T. Castaneum, Liposcelis bostrychophila, Coptotermes gestroi, Coptotermes curvignathus, etc.
[243].

3.14. The biological activity of individual groups of biologically active substances and individual compounds isolated from a. medicinal

A number of studies were carried out for individual biologically active substances isolated from alpinia rhizomes, as well as their groups.

3.14.1. Phenols and polyphenols

It is believed that molecules containing phenolic hydroxyl groups act as antioxidants due to their ability to donate hydrogen [45, 56, 57, 60, 70, 164, 184] and as prooxidants that contribute to their anticancer activity [111, 205].

The extract obtained by hot maceration with 50% ethanol contained significantly more phenol and flavonol, and also showed significantly higher antibacterial activity againstBacillus cereus, Staphylococcus aureus, Pseudomonas aeruginosa and Escherichia coli versus similarethanol extract obtained by cold maceration [215].

The first extract also showed better antioxidant activity compared to the second, inhibiting the free DPPH radical with moderate reducing capacity, compared to ascorbic acid as the reference antioxidant. At the same time, none of the extracts showed antifungal activity againstAspergillus niger and Candida albicans [215].

Interestingly, ethanol extract A. officinarum (95% ethanol, infusion at 70 ° C for 6 hours) also had a higher total phenol and flavonoid content compared to aqueous extract, but its antioxidant activity (using DPPH analysis) was significantly lower [197].

Flavonoids. The flavonoid fraction obtained by [256] by purifying the ethanol extract of rhizomes a. medicinal using macroporous adsorption resins [68], containing 5 flavonoids (comp. No. 1.2., 1.5., 1.6., 1.9., 5.2. [20]), showed antiproliferative activity through apoptosis of cells caused by the mitochondrial pathway [55] ...

Flavonoids galangin, quercetin and kaempferol from rhizomes a. drug named as the main polyphenols with antifungal action [207]. The flavonoids quercetin, kaempferol, and galangin also play the main role in protection against oxidative stress due to the expression of antioxidant proteins [113].

Quercetin can promote osteoblast differentiation and inhibit osteoclastogenesis bysuppression of mRNA gene expression RANKL in osteoblasts and therefore inhibit the functionosteoclasts [206].

Galangin has a pronounced antioxidant effect, neutralizes free radicals [252] and experimentally reduces acute lung damage caused by lipopolysaccharides [209], damage to the liver [210] and kidney [211] of rats caused by fructose. Moreover, galangin can prevent the destruction of osteoclastic bone and inhibit osteoclastogenesis by weakeningRANKLinduced N-terminal kinases c-Jun, p38 and activation of nuclear kappaB factor in predecessorsosteoclasts, as well as in mice with collagen-induced arthritis [123].

Flavonol galangin (comp. 1.5 - Fig. 1 [20]) is the dominant compound in all morphological groups of raw materials A. officinarum, showing anti-inflammatory, antioxidant andanticancer properties, as well as inhibition of the production of NO and enzymes [77, 118, 149, 169, 170, 224, 250, 254, 256].

Quite a lot of studies are devoted to the study of the specific pharmacological activity (anticancer, antibacterial, enzyme-inhibiting, etc.) of galangin, as well as the mechanisms of its action [63, 106, 107, 124, 144, 159, 252, 258]. The following types of action have been established experimentally: anti-cancer [63, 88, 107, 159, 252, 258], anti-inflammatory [132, 160], antibacterial [73, 144],

inhibitory enzymes [106], antiulcer [100, 233], pronounced antioxidant [118, 235, 258]. However, the molecular mechanism of its action, which underlies the observed pharmacological effects, is still little known [55]. It has only been reported that flavonoids act by suppressing the function of the cytoplasmic membrane, such as altering the influx of calcium, which contributes to the destruction of the cell membrane [50, 199, 214, 242]. There is also evidence that phenols and, in particular, flavonoids are able to penetrate into the hydrophobic layer of the cell membrane, causing disruption of the lipid packing of the membrane [50, 86, 138].

When studying the mechanisms of the antiulcer action of galangin [100], we took into account its ability to inhibit degranulation of human neutrophils [134], reduce the levels of TNF-α, IL-1β, and IL-6 mRNA [132, 210], and bind to COX-2, as shown the results of the study of molecular docking [118].

The results of these studies allowed Gong J. et al. (2018) suggest that galangin may be a potent antiulcer compound. On the model of indomethacin-induced gastric damage in rats, the researchers found that the antiulcer effect really exists not only for extracts (Section 3.9), but also for pure galangin. It is realized through cyclooxygenase and noncyclooxygenase pathways [100].

When studying the antitumor effect, it was shown that galangin induces apoptosis in hepatocellular carcinoma cells via the mitochondrial pathway of caspase 8 / t-Bid [255].

DAG isolated from A. officinarum [20], are of particular interest for research and development of drugs, dietary supplements for food and SPP due to their diverse and significant biological types of action: anti-inflammatory [169], antioxidant [137], antibacterial and antifungal [258], antiviral [62, 157] and hepatoprotective, neuroprotective [157, 241], antitumor [49, 157], inducing apoptosis, S-phase arrest, and differentiation in human neuroblastoma cells [223].

According to [55], due to the presence of DAG, the ethanol extract of the rhizomes of a. drug possessed in the experiment powerful anti-inflammatory, anticarcinogenic, antinociceptive and antipsychiatric activity in the model of carrageenan edema of the paw [145, 245, 249].

For DAG a. the drug has a cytotoxic effectin vitro against several linescancer cells [154]. Individual DAGs were isolated from the dried ethanol extract using ethyl acetate. The compound 1,7-diphenylhept-4-en-3-one (No. 5.8. [20]) showed cytotoxicity against the human glioblastoma T98G cell line with IC_{50} 27 μmol / L, while the compound alpinin B (No. 5.9. [20]) was inactive against the tested cell lines (cell lines of murine glioblastoma melanoma T98G and B16-F10) [155].

Compound alpinin C (No. 5.10. [20]) showed selective cytotoxicity against human breast cancer. MCF-7 and human glioblastoma T98G cell lines and compound 5-hydroxy-1- (4-hydroxy-3-methoxyphenyl) -7-phenylhepta-4,6-dien-3-one (# 5.11) showed significant cytotoxicity against hepatoma human HepG2 cells, human breast cancer MCF-7, human glioblastoma T98G, and human melanoma cell line B16 – F10 with IC values$_{50}$ 8.46, 12.37, 22.68, and 4.44 μmol / L, respectively [154].

Dimeric DAGs (No. 5.9. And 5.10.) Showed only selective or low cytotoxicity, which may be associated with the absence of its α, β-unsaturation in its molecular structure [154]. It is important that the α, β-unsaturated unit is defined aspi-bond between α and β carbon atoms adjacent tocarbonyl (= CO) group [212], and is often used as an active component in the development of enzyme inhibitors [130]; therefore, Basri AM et al. considers it necessary to continue further biological studies of new dimeric DAG compounds [55].

When studying the cytotoxicity of DAH A. officinarum Sun Y. et al (2008) showed that DAH induces moderate antiproliferative effects (IC_{50} = 6-10 μg / ml) on HepG2, MCF-7 and SF-268. In colon cancer, the mechanism of action is due to the suppression of the Wnt / β-catenin pathway [43, 222].

In addition to these works, the antitumor activity of DAH A. officinarum is discussed in reviews [55, 193, 199] and is confirmed by numerous experimental studies [49, 157].

According to [251], 13 DAHs from ethanol extract of rhizomes A. officinarum also possessantibacterial activity against Helicobactor pylori. In particular,3 new compounds of DAG-nature [20] have shown a particularly strong antibacterial effect
against the Hp-Sydney 1 strain with MIC values of 9–12 μg / ml, as well as against the Hp-F44 strain - with MIC values of 25–30 μg / ml [251].

The antioxidant and neuroprotective properties of DAGs and their adducts are also described in detail in Sections 3.6 and 3.7, respectively.

Phenylpropanoids. Basri AM et al. (2017) revealed differences in the antioxidant behavior of phenylpropanoid compounds [55] (No. 6.1., 6.2., 7.1. – 7.5. [20]). In particular, their activity may

influence the number of hydroxyl groups present in the molecule [162].

3.14.2. Terpenes

A team of researchers from the Federal University of Rio de Janeiro (Brazil) [230] and a number of other researchers [125] reported on the antimicrobial effect of essential oil from raw materials of various species of the genus Alpinia as one of the main types of biological activity caused by terpenoids. For a. medicinal, this effect is confirmed in works [55, 158]. The antibacterial effect is explained by the fact that extracts of small galangal can penetrate into the bacterial cell, causing rupture of the bacterial membrane, which leads to the death of this cell [198].

It has also been reported that terpenes act by suppressing the function of the cytoplasmic membrane, such as altering the influx of calcium, which contributes to the destruction of the cell membrane [50, 199, 214, 242].

In 2016, Wen T. et al. singled out from a. medicinal, two new diterpene compounds with antioxidant and anti-inflammatory effects, which may be associated with inhibition of reactive oxygen species (ROS): (12S) -15-16-epoxy-8 (17), 13 (16), 14-labdatrient-12-ol (No. 11.1. [20]) and (12 E) -labda-8 (17), 12 (13) -diene-15,16-olide (No. 11.2. [20]). Extraction was carried out with petroleum ether from ethanol (95%) extract of rhizomes [236].

ROS can cause damage to cells and tissues, activate oxidative stress, and cause inflammation [184, 201, 229]. This leads to a wide range of disorders and diseases, including inflammatory, cardiovascular, and neurodegenerative [91, 176, 200]. Therefore, 2 labdan diterpenes were recognized by experts as very promising compounds, especially with regard to their antioxidant and anti-inflammatory activity in the treatment of socially significant diseases [55].

In the same year from rhizomes A. officinarum, a new labdan-type diterpene (Z) -12,14-labdadiene-15 (16) -olide-17th acid (No. 12.1. [20]) and a new natural sesquiterpene cadinan, 4-isopropyl-6-methyl-1-naphthalenemethanol (No. 12.2. [twenty]). New compounds were isolated by the authors along with galangin, kaempferol, and quercetin [259].

According to experts, a wide range of pharmacological actions suggests that labdan-type diterpenes may significantly affect immune system function and inflammatory responses. Many labdan diterpenes have antimicrobial, enzymatic, and endocrine properties, and also exhibit a pronounced effect on cancer cells, demonstrating antiproliferative and cytotoxic activity [80]. However, in the described study, compounds No. 12.1. and 12.2. [20] did not demonstrate significant cytotoxic activity against the HeLa and HepG2 cancer cell lines with IC_{50} > 50 μg / ml^{-1} [259].

4. Application of Alpinia officinarum in modern world medical and pharmaceutical practiceAccording to official data (approved by Commission E), a. medicinal has antispasmodic, anti-inflammatory and antibacterial properties; indications for the use of rhizomes are dyspeptic complaints and loss of appetite [147]. According to the official medical handbook "PDR for Herbal Medicines", unproven indications for use (from traditional medicine) include: Remheld syndrome (pain in the upper abdomen of a complex type), sluggish digestion, as well as liver and gallbladder diseases (basic) , fever and colds, cough / bronchitis, infection tendency and inflammation in the oral cavity and pharynx (additional); in modern Chinese medicine drugs a. the drug is used for pain, especially in the stomach [104, 147].

In many European countries, tincture or powder of rhizomes of medicinal galangal are included in gastric and mouth-watering drops and preparations that tone the stomach [39]. Various extracts (alcohol, water, teas) of rhizomes a. medicinal is used for loss of appetite, lack of gastric juice, with a lack of enzymes in the intestine and with stagnation in the gallbladder, treats impotence [1].

In particular, it is reported that in Western European medicine, small galangal is used in the form of tea: 2 teaspoons of chopped rhizomes per 1 cup of boiling water, leave for 5 minutes, filter and drink without sugar in warm form in small sips 3 times a day half an hour before meals. Tea is recommended for loss of appetite, achilia, gallbladder atony [11].

In modern herbal medicine (with taking into account information about antitoxic, tonic, immunomodulatory, positive gonadotropic, anabolic action) small galangal (synonym for A. medicinal), like other representatives of this family. Ginger (ginger, turmeric), are prescribed in combination with different ingredients "cold natures", which include the vast majority of patients with multiple sclerosis [3] and cancer patients [37].

According to O.D. Barnaulov (2015), galangal is indicated for liver diseases and hemorrhoids. With wine, it promotes weight gain, “which is what hypotrophic girls and women with clearly visible collarbones strive for,

ribs ". In addition, in combination with adaptogens and tonics, it can be considered as a constitutional remedy for asthenics, hypotonic, hypotrophic, often and long-term ill people, patients with problems in the reproductive sphere [3].

Generalized ideas about the possibility of using a. medicinal in modern (first decade of the XXI century) medico-pharmaceutical practice were presented by D. Duke JA in the Handbook of Medicinal Herbs [81], as well as in the CRC handbook of medicinal spices [83] (Table 4).

According to later data [207], the rhizomes of a. medicinal refers to aromatic, gastric, stimulant and carminative; are used to relieve flatulence, improve digestion and prevent vomiting from indigestible food, and help reduce polyuria in diabetes [207]. According to G.Das et al. (2020), small galangal is used in herbal medicines for the treatment of hemorrhoids, menstrual irregularities, inflammatory diseases of various origins and localization, as well as for discomfort in the abdominal region [75].

Table 4

Indications for use a. medicinal in alphabetical order (according to [81])

No. p / p	Indications for application	Evidence-based base	P / p No.	Indications for use	Evidence-based base
1	Adenopathy	f; HHB; MAD	25	Fever	2; DAA; GMH; PHR; PH2
2	Amenorrhea	f; MAD	26	Malaria	f; EFS
3	Anemia	f; MAD	27	Flatulence	f; EFS; MAD; PNC
4	Anorexia	2; DAA; KOM; MAD; PH2	28	Urolithiasis disease	f; MAD
5	Bacterial defeat	1; KOM; PH2	29	Tumors, malignant tumors	1; PNC
6	Pain - pain syndrome	f; PH2	thirty	Swelling, swelling	f; HHB
7	Sore throat	f; DEP	31	Polyuria	f; DEP
eight	Pain in the stomach and abdomen	f; DAA; MAD; PH2	32	Colds	2; PHR; PH2
nine	Bronchitis	2; PHR; PH2	33	Pulmonosis - diseases of the respiratory system	f; MAD
ten	Freckles	f; DEP	34	Rheumatism	f; MAD
eleven	Inflammatory diseases	2; KOM; PHR; PH2	35	Remkheld's syndrome is a set of symptoms characteristic of a malfunction of the cardiovascular system and gastrointestinal tract.	f; PH2
12	Halitosis (unpleasant smell from the mouth)	f; DEP	36	Syncope - fainting, bouts of short-term loss consciousness caused by temporary disturbance cerebral blood flow	f; DAA; HHB
13	Gastritis	f; GMH	37	Stomatitis	2; PHR; PH2
fourteen	Hepatosis - non-inflammatory bodily diseases liver caused by exogenous or inherited venous factors	2; DAA; PHR; PH2	38	Convulsions	2; KOM; PH2
15	Dizziness	f; HHB	39	Nausea, motion sickness	f; DAA; GMH; MAD
16	Diarrhea	f; DAA; MAD	40	Cancer	1; JLH; PNC
17	Dysmenorrhea	f; DAA; HHB; MAD	41	Bladder cancer	f; JLH
eighteen	Dyspepsia	2; DAA; GMH; KOM; PH2	42	Penile cancer	f; JLH
19	Cholelithiasis	f; MAD	43	Vomit	f; GMH
twenty	Toothache	f; DAA; HHB	44	Pharyngitis	2; PHR; PH2

21	Infections	f; PH2	45	Cholera	f; DAA
22	Hypochondria	f; DAA	46	Cholecystitis	2; MAD; PHR; PH2
23	Qatar	f; GMH	47	Enteritis	f; DAA; PH2
24	Colic	f; PHR	48	Ulcers	1; PNC

Official dosage forms (according to PDR) are: crushed rhizome, powder and other galenic preparations for oral administration. The daily dose is 4 g of rhizome. To prepare the infusion, 0.5–1 g of crushed raw materials are poured with boiling water and filtered after 10 minutes; take 1 glass 30 minutes before meals [147]. According to [81, 83], the crushed rhizome should be brewed in a cup at a dose of 0.5–1 g of rhizomes per 1 cup (from 1 to 4 times a day) [93, 104] or rhizome powder should be used in a single dose of 0.5 –1.5 g [152], according to other sources - 0.62–1.25 g [165]. The tincture should be used in a single dose of 1-2 g [152] or 1.5-2 g several times a day [165], according to other sources - in a daily dose of 2-4 g [58].

5. Safety assessment a. medicinal: potential toxicity, contraindications for use, side effects

5.1. Official safety data

Rhizome and alpinum extract are traditionally considered safe remedies, since they have been used for the treatment of various diseases in China for hundreds of years [61, 145, 218]. According to official data (approved by Commission E), a. the drug carries no health risks or side effects when the prescribed therapeutic doses are used correctly [104, 147], and dangerous or side effects for the appropriate therapeutic dosages have not been reported [81, 83].

5.2. Potential toxicity

According to D. Duke (2002, 2003, 2006), the rhizome of a. medicinal and all extracts from it belong to the 1st class of toxicity (non-toxic) [81, 83, 172].

A more recent study of the acute and subchronic toxicity of the extract (95% ethanol) of rhizomes a. drug was performed by a group of researchers from Saudi Arabia and Egypt before conducting an experimental study of the antitumor activity of this extract. The statistical evaluation of the results was carried out in full [44].

The experimental study was carried out on Swiss albino mice of both sexes (35–38 g) purchased from the vivarium of the Alazahar University (Cairo, Egypt). The animals were kept in polypropylene cages under standard environmental conditions [187].

10 g of a previously prepared [44] dried alcoholic extract of rhizomes was dissolved in fresh distilled water using the emulsifier Tween 80 according to [85], and then orally administered to rats [44].

Medium lethal dose of alcoholic extract A. officinarum for oral administration (LD_{50}) was determined according to [64]. The investigated extract was evaluated at a dose of 4000 mg / kg. However, there were no signs of toxicity or death of animals within 24 hours [44]. Therefore, the extract has been classified as a safe product for human use [44, 187].

To study subchronic toxicity [44], an alcoholic extract at a dose of 400 mg / kg was used, which was administered orally for 35 days, n = 10, and side effects on liver and kidney function were assessed according to [85]. Liver enzymes were determined in serum, as well as urea and creatinine as indicators of renal function according to [85].

The study of subchronic toxicity also showed the absence of toxicity of the studied extract of rhizomes [44]. The administered daily therapeutic dose (400 mg / kg) did not show any changes in liver and kidney function markers (Table 5). This means that the plant extract is neither hepatotoxic nor nephrotoxic [204].

5.3. Contraindications

According to some sources, there are no contraindications to the use of small galangal [39]. According to other sources, rhizome and preparations from it are not recommended for use in gastric ulcer and duodenal ulcer, in peptic esophagitis, ulcerative colitis, colon diverticulosis [1], atonic constipation [13]. With regard to use during pregnancy, the data are contradictory: from a complete ban [1] to indications of harmlessness [81]. According to Ayurvedic beliefs, it is not recommended for pregnant women in large doses [15].

Alcohol tincture of small galangal should not be used during pregnancy, as well as for children and people,

prone to alcoholism [13].

The drugs can reduce capillary permeability and lead to vasoconstriction, therefore, in high doses, they are contraindicated in hypertension and with high prothrombin index [13].

In TCM, the use of drugs from a. drug is contraindicated for pain in the epigastric region caused by an excess of Fire in the Liver and Stomach, and vomiting due to Fire in the Liver and Stomach [7, 8].

5.4. Adverse reactions and overdose

A significant overdose of Chinese galangal can provoke severe abdominal pain [13] diarrhea, nausea [1] and vomiting [1, 13].

5.5. Precautionary measures, associated with the lack of domestic regulatory documents for raw materialsDespite the fact

that the domestic regulatory documents for raw materials a. medicinal is not yet available, the experience of long-term safe food and traditional medical use, as well as the results of experimental studies allow the use of rhizomes of a. medicinal and their extracts as ingredients of drugs, dietary supplements and SPP.

CONCLUSION

Increasing interest in experimental and clinical research a. medicinal on the part of the world scientific community is due to a significant amount of accumulated ethnobotanical and ethnopharmacological material. Considering the long experience of safe traditional use, as well as the almost thorough phytochemical knowledge of a. medicinal and the availability of reliable results of preclinical and clinical studies [75], it is advisable to take into account the opinion of the international expert community on the high nutraceutical potential and good prospects for widespread use of this plant in the world medico-pharmaceutical practice.

CONCLUSIONS

1. The carried out information and analytical research allowed to establish a proven efficacy and safety of rhizome extracts a. medicinal, which is confirmed by the centuries-old food use and the successful use of the plant, both in traditional medicine in different countries, and in modern world medical and pharmaceutical practice.

2. Revealed works describing the mechanisms of action of biologically active substances a. medicinal, as well as processes, causing antitumor and some other established biological effects. No toxic effects were found.

3. Along with high efficiency, some studied BAS exhibit selectivity, which allows consider them as promising sources for the creation of natural medicines, dietary supplements for food and SPP.

4. The main groups of biologically active substances responsible for a wide range of pharmacotherapeutic actions rhizomes a. medicinal, phenols (flavonoids, DAGs, phenylpropanoids), terpenes, phytosterols and adducts of DAG-terpene nature can be considered.

5. Phenolic fraction obtained using various solvents, as well as individual biologically active substances, including adducts of DAG and terpenes, exhibit pronounced antiproliferative, antioxidant, anti-inflammatory, antiviral, neuroprotective, antiosteoporotic, antiulcer, antihyperlipidemic action.

6. Terpenes (including diterpenes) are mainly responsible for the antimicrobial, anti-inflammatory, antiproliferative, antiviral action.

7. The results obtained indicate a high nutraceutical potential and good prospects for the use of small galangal in the world medicopharmaceutical practice as a source of drugs, dietary supplements and SPP.

LITERATURE

1. Alpinia officinalis - Alpinia officinalis, alpinia officinalis // Handbook of homeopathy [Electronic resource]. - Access: http://med.niv.ru/doc/dictionary/homeopathy/fc/slovar-192-2.htm (as of 04/29/2020)

2. Amasiatsi, A. Unnecessary for the ignorant / A. Amasiatsi. - M .: Nauka, 1990. - T.13. - 880 p.

3. Barnaulov, O.D. Medicinal properties of spices. 2nd ed. revised and add. / O.D. Barnaulov. - Sub .: Inform-Navigator, 2015 .-- 288 p.

4. Medicinal properties of spices / OD. Barnaulov, M.L. Pospelova, S.O. Barnaulova, A.S. Benhammadi. - SPb .: Publishing house of the Foundation of Russian Poetry, 2001 .-- 240 p.

5. Belodubrovskaya, G.A. Nomenclature of homeopathic remedies: Methodical. allowance / G.A. Belodubrovskaya, E.V. Zdanevich; Under total. ed. prof. K.F. Blinova. - SPb: SPGKhFA, 1996 .-- 32 p.

6. Belodubrovskaya, G.A. Nomenclature of medicinal plants used in homeopathy: Methodical. Manual / G.A. Belodubrovskaya, E.V. Zhokhova. - SPb .: SPbKhFA, 1998 .-- 59 p.

7. Belousov, P.V. Alpinia officinalis rhizome - Rhizoma Alpiniae Officinari / P.V. Belousov // Illustrated Atlas of Chinese Medicine Medicines: Medicines Warming Internal Organs [Electronic resource]. - Access: http://belousov.kz/atlas/124.html (as of 28.04.2020)

8. Belousov, P. V. Fundamentals of Chinese herbal medicine / P.V. Belousov, A.V. Chemeris. - Almaty, 2010 .-- 198 p.

9. The value of the chemical properties of nitric oxide for the treatment of cancer / D.A. Wink, J. Vodovoz, J.A. Cook [et al.] // Biochemistry. - 1998. - Issue 7. - pp. 948–957.

10. Vinogradov, N.A. The Many Faces of Nitric Oxide / N.A. Vinogradov // Russian Journal of Gastroenterology, hepatology, coloproctology. - 1997. - No. 2. - P.6-11.

11. Galanga // Handbook of homeopathy [Electronic resource]. - Access: https://homeopathy.academic.ru/1222/Galanga_-_Galanga%2C_Alpinia_drug (as of 15.02.2020)

12. Galanga // Brockhaus and Efron Encyclopedic Dictionary: in 86 volumes (82 volumes, 4 additional). - SPb., 1890-1907. - T. 7A (14): Vygovsky - Galban. - 1892 .-- 952 s. (P. 887).

13. Galanga // Encyclopedia of Spices [Electronic resource]. - Access: http://www.trapeza.tv/enc/enc_list.php?enc=28 (accessed 10/02/2020)

14. State Register of Medicines (VII annual periodical). - M .: Technical book, 2002 .-- 1301 p.

15. Grischuk, N.A. The world of spices and spices / N.A. Grischuk. - Lutsk: Drukmarket, 2010 .-- 192 p.

16. Gubanov, I.A. Medicinal plants and mushrooms used in homeopathy. Quick reference / I.A. Gubanov, A.V. Patudin, A.M. Rabinovich. - M .: Homeopathic center, 1995 .-- 112 p.

17. Dudchenko, L.G. Spicy-aromatic and spicy-flavoring plants: Handbook / otv. ed. K. M. Sytnik (Academy of Sciences of the Ukrainian SSR) / L.G. Dudchenko, A.S. Koziakov, V.V. Krivenko. - K .: Naukova Dumka, 1989 .-- 304 p. - (Galgant. - pp. 28–49).

18. Medicinal plants used in homeopathy and domestic raw material base for production homeopathic medicines / T.L. Kiseleva, A.A. Karpeev, I.A. Samylina, A.V. Nefedova // In the book. Homeopathic pharmacy: introduction and guidance / comp. Kiseleva T.L., Karpeev A.A. - M .: Publishing house of FNCEC TMDL Roszdrav, 2005. - P.228–438.

19. Kiseleva, T.L. Alpinia officinalis (Alpinia officinarum) in traditional medicine and modern medical and pharmaceutical practice. Publication 1: botanical characteristics, synonymy, peculiarities of raw material procurement, food use / T.L. Kiseleva, N.V. Coleman // Traditional Medicine. - 2020. - No. 2 (61). - pp. 20–35.

20. Kiseleva, T.L. Alpinia officinalis (Alpinia officinarum) in traditional medicine and modern medical and pharmaceutical practice. Publication 2: chemical composition and biologically active substances causing pharmacotherapeutic action / T.L. Kiseleva, N.V. Coleman // Traditional Medicine. - 2020. - No. 3 (62). - pp. 15–32.

21. Kiseleva, T.L. Nomenclature of producing plants and raw materials for the production of homeopathic medicines in Russia. Reference manual / T.L. Kiseleva, E.V. Tsvetaeva. - M .: Publishing house of the SPC of traditional medicine and homeopathy of the Ministry of Health of the Russian Federation, 2002. - 124 p.

22. Lad, V. Herbs and spices / V. Lad, D. Frawley; Per. from English - M .: Sattva, 2000 .-- 304 p.

23. Protective and damaging effects of periodic hypoxia: the role of nitric oxide / E.B. Manukhin, H.F. Downey, R.T. Mallet, I.Yu. Malyshev // Bulletin of Ros. AMN. - 2007. - No. 2. - pp. 25–33.

24. MoH and MP RF: On the use of the method of homeopathy in practical health care / Order from 11/29/95, No. 335.

25. Mikonenko, A.B. Phytotherapy in Traditional Chinese Medicine / A.B. Mikonenko. - M .: Profit Style, 2010 .-- 304 p.

26. One of the Men. On the properties of herbs (translated from Latin and commentary by YF Schultz) / Odo iz Mena; Under total. ed. V.N. Ternovsky. - M .: Medicine, 1976 .-- 272 p.

27. O'Connell, J. Encyclopedia of Spices. From Anise to Saffron / J. O'Connell; Per. from English E.N. Kruchins. - M .: Eksmo, 2018 .-- 352 p.

28. Pokhlebkin, V.V. Kalgan / V.V. Pokhlebkin // In the book: Great Encyclopedia of Culinary Arts. - M .: Publishing house: Tsentrpoligraf, 2009 .-- 975 p.

29. Pokhlebkin, V.V. All about spices / V.V. Pokhlebkin. - M .: ZAO Tsentrpoligraf, 2010 .-- 207 p.

30. Pokhlebkin, V.V. Spices / V.V. Pokhlebkin // In the book: Culinary Dictionary. - M .: Publishing house "E", 2015. - 456 s.

31. Pokhlebkin, V.V. Culinary Dictionary / V.V. Pokhlebkin. - M .: Publishing house "E", 2015. - 456 p.

32. Pokhlebkin, V.V. Big cookbook / V.V. Pokhlebkin. - M .: Publishing house "E", 2017. - 992 p.

33. Sayfutdinov, R.G. The role of nitric oxide in diseases of internal organs (review) / R.G. Sayfutdinov // Bulletin of modern clinical medicine. –2009. - No. 3. - S. 48–53.

34. Sy, H. Fundamentals of Chinese medicine / H. Sy, L. Luzin, Ts. Sy. - M .: Medicine, 2009. –660 p.

35. Upur, H. Secrets of Chinese medicine / H. Upur, V.G. Started. - SPb: Publishing house im. A.S. Suvorin, 1992 .-- 204 p.

36. Halpern, M. Lessons on the path of Ayurveda / M. Halpern; Per. from English - M .: Sattva, 2017 .-- 256 p.

37. Choyzhinimaeva, S.G. Tibetan recipes for health and longevity / S.G. Choyzhinimaev. - M .: Eksmo Publishing House, 2017 .-- 384 p.

38. Shedo, A. Spices / A. Shedo, I. Kreich. - Bratislava, 1985 .-- 252 p.

39. Schreter, A.I. Natural raw materials of Chinese medicine. T. 1 / A.I. Schreter, B.G. Valentinov, E.M. Naumova. - M .: "Terevinf", 2004. - 506 p.

40. Shubin, V.E. EPR study of the formation of nitric oxide during the reduction of nitrofurans and nitroimidazoles. I. Solutions of hemoglobin / V.E. Shubin, Z. V. Kuropteva // Studia biophysica. - 1983. - Vol. 97. - No. 2. - P.157-164.

41. Stored-product insects in botanical warehouses / AY Abdelghany, SS Awadalla, NF Abdel-Baky [et al.] // J. Stored Prod. Res. - 2010; 46: 93-97.

42. Cyclooxygenase-2 selectivity of non-steroidal anti-inflammatory drugs and the risk of myocardial infarction and cerebrovascular accident / NS Abraham, HB El-Serag, C. Hartman [et al.] // Aliment. Pharmacol. Ther. - 2007; 25: 913-924.

43. A review on the ethnomedicinal uses, phytochemistry and pharmacology of Alpinia officinarum Hance / IB Abubakar, I. Malami, Y. Yahaya, SM Sule // J. Ethnopharmacol. - 2018; 224: 45-62.

44. Analysis of Alpina officinarum Hance, chemically and biologically / FA Alasmary, EA Assirey, RM El-Meligy [et al.] // Saudi Pharm J. - 2019 Dec; 27 (8): 1107-1112. Published online 2019 Sep 25.

45. Structural features, kinetics and SAR study of radical scavenging and antioxidant activities of phenolic and anilinic compounds / HM Ali, A. Abo-Shady, HA Sharaf Eldeen [et al.] // Chem. Cent. J. - 2013; 7: 53.

46. Blepharocalyxins C – E: three novel antiproliferative diarylheptanoids from the seeds of Alpinia blepharocalyx / MS Ali, Y. Tezuka, AH Banskota, S. Kadota // Tetrahedron letters. - 2000; 41 (31): 5903-5907.

47. Alpinia officinarum // Wikipedia [Electronic resource in English. language]. - Access: https://en.wikipedia.org/wiki/Alpinia_officinarum (as of 01/25/2020).

48. Altman, RD Effects of a ginger extract on knee pain in patients with osteoarthritis / RD Altman, KC Marcussen // Arthritis Rheuma. - 2001; 44: 2531-2538.

49. Diarylheptanoids from the rhizomes of Alpinia officinarum and their anticancer activity / N. An, ZM Zou, Z. Tian [et al.] // Fitoterapia. - 2008; 79: 27-31.

50. Anand David, AV Overviews of Biological importance of Quercetin: A Bioactive Flavonoid / AV Anand David, R. Arulmoli, S. Parasuraman // Pharmacogn. Rev. - 2016; 10: 84-89.

51. Aruoma, OI Assessment of potential prooxidant and antioxidant actions / OI Aruoma // J. Amer. Oil Chem. Society. - 1996; 73 (12): 1617-1625.

52. Novel Compounds with new Anti-Ulcergenic Activity from Convolvulus pilosellifolius using Bio-Guided Fractionation / SA Awaad, A. Al-Refaie, RM El-Meligy [et al.] // Phytother. Res. 2016; 30: 2060–2064.

53. Quantitative and qualitative analysis for Standardization of Euphorbia cuneata Vahl / SA Awaad, MR Alothman, YM Zain [et al.] // Saudi Pharmaceut. J. - 2018; 25: 1175-1178.

54. Awang, D. Ginger / D. Awang // Can Pharm J. 1992; 125: 309-311.

55. Basri, AM A review on the pharmacological activities and phytochemicals of Alpinia officinarum (Galangal) extracts derived from bioassay-guided fractionation and isolation / AM Basri, H. Taha, N. Ahmad // Pharmacogn. Rev. - 2017; 11 (21): 43–56.

56. Baumann, J. Prostaglandin synthetase inhibiting O_2-radical scavenging properties of some flavonoids and Related phenolic compounds / J. Baumann, G. Wurn, FV Bruchlausen // Naunyn-Schmiedebergs Arch. Pharmacol. - 1979; 308: 27-32.

57. Antioxidant and structure-activity relationships (SARs) of some phenolic and anilines compounds / E. Bendary, RR Francis, HM Ali [et al.] // Ann Agric Sci. - 2013; 58: 173-181.

58., The Complete German Commission E Monographs: Therapeutic Guide to Herbal Medicines, American Botanical Council, Austin, TX and Integrative Medicine Communications / M. Blumenthal [et al.]; Eds. - Boston, MA, 1998.

59. Bown, D. The Royal Horticultural Society Encyclopedia of Herbs and Their Uses / D. Bown. - London: Dorling Kindersley Limited, 1995 .-- 424 p.

60. Brewer, MS Natural antioxidants: Sources, compounds, mechanisms of action, and potential applications /

MS Brewer // Compr. Rev. Food Sci. Food. Saf. - 2011; 10: 221-247.

61. Bu, X. Chemical study of Alpinia offcinarum / X. Bu, G. Xiao, L. Gu // Zhong Yao Cai. - 2000; 23: 84-87.

62. Byler, KG In-silico screening for anti-Zika virus phytochemicals / KG Byler, IV Ogungbe, WN // J. Mol. Graph. Model. - 2016; 69: 78-91.

63. Galangin inhibits cell invasion by suppressing the epithelial-mesenchymal transition and inducing apoptosis in renal cell carcinoma / J. Cao, H. Wang, F. Chen [et al.] // Mol. Med. Rep. - 2016; 13: 4238-4244.

64. Carocho, M. The role of phenolic compounds in the fight against cancer - a review / M. Carocho, ICFR Ferreira // Anti-Cancer Agents Med. Chem. - 2013; 13: 1236-1258.

65. Chang, CL Phytochemical Composition, Antioxidant Activity, and Neuroprotective Effect of Terminalia chebula Retzius Extracts / CL Chang, CS Lin // Evid. Based Complement. Alternat. Med. - 2012; 2012: 125247.

66. Chang, CL Phytochemical characteristics, free radical scavenging activities, and neuroprotection of five medicinal plant extracts / CL Chang, CS Lin, GH Lai // Evid. Based Complement. Alternat. Med. –2012: 984295. - Published online 2011 Aug. ten.; 2012 Article ID 984295.8 p.

67. Clemett, D. Raloxifene: a review of its use in postmenopausal osteoporosis. Drugs / D. Clemett, CM Spencer. - 2006; 60: 379-411.

68. CN104138368A. Preparation method and cancer treatment effect of rhizome Alpiniae officinarum aboveground part AO-95; 12 November. - 2014.

69. Protective effects of methyl gallate on H_2O_2-induced apoptosis in PC12 cells / JA Crispo, M. Piché, DR Ansell [et al.] // Biochemical and Biophysical Research Communications. - 2010; 393 (4): 773-778.

70. Crouzet, J. Glycosidically bound volatiles in plants / J. Crouzet, D. Chassagne // In: Ikan R., editor. Naturally Occurring Glycosides. - Chichester, England: John Wiley and Sons Ltd, 1999. - P. 225-274.

71. Salvianolic acid B prevents bone loss in prednisone-treated rats through stimulation of osteogenesis and bone marrow angiogenesis / L. Cui, T. Li, Y. Liu [et al.] - PLoS One. 2012; 7: e34647.

72. Culpeper Nicolas. Complete Herbal (1653) / Nicolas Culpeper. - Wordsworth, 1995. - P.313-314.

73. Aggregation of Staphylococcus aureus following treatment with the antibacterial flavonol galangin / TPT Cushnie, VES Hamilton, DG Chapman [et al.] // J. Appl. Microbiol. - 2007; 103: 1562-1567.

74. A prospective study of postmenopausal hormone use and ovarian cancer risk / KN Danforth, SS Tworoger. JL Hecht [et al.] // Br J Cancer. 2007; 96: 151-156.

75. Galangal, the multipotent super spices: A comprehensive review / G. Das, JK Patra, S. Gonçalves [et al.] // Trends in Food Science and Technology. - 2020; 101: 50-62. (2020).

76. Das, K. Techniques for evaluation of medicinal plant products as antimicrobial agent: Current methods and future trends / K. Das, RK Tiwari, DK Shrivastava // J. Med. Plants Res. - 2010; 4: 104-111.

77. Deng, YF Determination of the content of galangin in Alpinia officinarum Hance harvested in different months by RP-HPLC / YF Deng, LN Feng, H. Luo // Chin. Pharm. J. - 2010; 45: 1593-1596.

78. Di Rosa, M. Studies on the mediators of acute inflammatory responses induced in rats in different sites by carrageenan and turpentine / M. Di Rosa, JP Giroud, DA Willoughby // J. Pathol. - 1971; 104: 15-29.

79. Ding, W. The main stratagems and technology for stored product pest control in ancient China / W. Ding, H. Liu, LS Li // J. Southwest Agric. Univ. - 2000; 22: 335-338.

80. Diterpenes labdane // Big Chemical Encyclopedia: chemical substances, components, reactions, process design [Electronic resource in English. language]. - Access: https://chempedia.info/info/labdane_diterpenes/ (as of 13.03.2020)

81. Duke, JA Handbook of Medicinal Herbs / JA Duke. - Boca Raton-London-New York-Washington: CRC Press, 2002. - 896 p.

82. Duke, JA Medicinal Plants of China, 2 vols. / JA Duke, ES Ayensu. - Reference Publications, Algonac, MI, 1985.

83. CRC handbook of medicinal spices / JA Duke, MJ Bogenschutz-Godwin, J. duCellier [et al.] - Boca Raton-London-New York-Washington, DC: CRC Press, 2003 .-- 333 p.

84. Resveratrol supplementation preserves long bone mass, microstructure, and strength in hindlimb-suspended old male rats / SM Durbin, JR Jackson, MJ Ryan [et al.] // J Bone Min Metab. - 2014; 32: 38-47.

85. Prophylactic and curative anti-ulcerogenic activity and the possible mechanisms of action of some desert plants / RM El-Meligy, AS Awaad, GA Soliman [et al.] // Saudi Pharmaceut. J. - 2017; 25: 387-396.

86. The interaction of flavonoids with membranes: potential determinant of flavonoid antioxidant effects / AG Erlejman, SV Verstraeten, CG Fraga, PI Oteiza // Free Radic. Res. - 2004; 38: 1311-1320.

87. Study on anti-obese and hypolipidemic effects of total flavonoids from Alpinia officinarum Hance in rats with nutritive obesity combined with hyperlipidemia / YJ Fang, DZ Xia, SW Wang, SS Ji // China Journal of Traditional Chinese Medicine and Pharmacy. - 2015; 30 (8), 2907-2910.

88. Chemopreventive mechanisms of galangin against hepatocellular carcinoma: A review / DY Fang, ZM Xiong, JM Xu [et al.] // Biomed. Pharmacother. - 2019; 109: 2054-2061.

89. Icariin protects against glucocorticoid-induced osteoporosis in vitro and prevents glucocorticoid-induced osteocyte apoptosis in vivo / R. Feng, L. Feng, Z. Yuan [et al.] // Cell Biochem Biophys. 2013; 67: 189-197.

90. Effect of glucocorticoid-induced oxidative stress on the expression of Cbfa1 / YL Feng, XL Tang // Chem Biol Interact. 2014; 207: 26–31.

91. Interrelation of oxidative stress and inflammation in neurodegenerative disease: role of TNF / R. Fischer, O. Maier // Oxid Med Cell Longev. - 2015.2015 610813.

92. Flannery, M. Avicenna / M. Flannery // Britannica [Electronic resource in English. language]. - Access: https: //www.britannica.com/biography/Avicenna (accessed 01.08.

93. PDR for Herbal Medicine, 1st ed. / T. Fleming [et al.] - Medical Economics Co., Montvale, NJ, 1998.

94. Gass, M. Preventing osteoporosis-related fractures: an overview / M. Gass, B. Dawson-Hughes // Am. J. Med. - 2006; 119: S3 – S11.

95. Epicalyxin F and calyxin I: two novel antiproliferatire diarylheptanoids from the seeds of Alpinia blepharocalyx / MB Gewali, Y. Tezuka, AH Banskota [et al.] // Organic letters 1999; 1 (11): 1733-1736.

96. In vitro antioxidant activity of Tectona grandis Linn / M. Ghaisas, V. Navghare, A. Takawale [et al.] // Pharmacol. Online. - 2008; 3: 296-305.

97. GHP (German Homoeopathic Pharmacopoeia); 5th ed. issued in 2001. - Deutscher Apotheker Verlag / Ad-Ex Translation Ltd, Medpharm Scientific Publishers, London: CRC Press, 2003 .-- 1772 p. - ISBN 3-88763-095-5

98. Ghil, S. Antiproliferative activity of Alpinia officinarum extract in the human breast cancer cell line MCF-7 / S. Ghil // Mol. Med. Rep. - 2013; 7: 1288-1292.

99. Ghosh, S. Alpinia: The gold mine of future therapeutics / S. Ghosh, L. Rangan // 3 Biotech. 2013; 3: 173.

100. Effects and possible mechanisms of Alpinia officinarum ethanol extract on indomethacin-induced gastric injury in rats / J. Gong, Zh. Zhang, X. Zhang [et al.] // Pharmaceutical Biology. - 2018; 56: 1, 294-301.

101. Effect of growth hormone therapy on nitric oxide formation in cystic fibrosis patients / C. Grasemann, F. Ratjen, D. Schnabel [et al.] // Eur. Respir J. - 2008. - Vol.31. - P.815-821.

102. Grieve, M. A Modern Herbal / M. Grieve. - New York: Hafner Press, 1931; Dover reprint, 2 vols, 1st reprinted 1971, Dover, New York

103. Gröblacher, B. Compounds of Alpinia katsumadai as potential efflux inhibitors in Mycobacterium Smegmatis / B. Gröblacher, O. Kunert, F. Bucar // Bioorganic & Medicinal Chemistry 2012; 20 (8): 2701-2706.

104. PDR for Herbal Medicines, 2nd ed. / J. Gruenwald [et al.]. - Medical Economics Co., Montvale, NJ, 2000.

105. Double directional adjusting estrogenic effect of naringin from Rhizoma drynariae (Gusuibu) / D. Guo, J. Wang, X. Wang [et al.] // J Ethnopharmacol. 2011; 138: 451–457.

106. Galangin, a flavonol derived from rhizoma Alpiniae officinarum inhibits acetylcholinesterase activity in vitro / AJ Guo, HQ Xie, RC Choi [et al.] // Chem. Biol. Interact. - 2010; 187: 246-248.

107. Galangin induces human colon cancer cell death via the mitochondrial dysfunction and caspase-dependent pathway / TK Ha, ME Kim, JH Yoon [et al.] // Exp. Biol. Med. (Maywood). - 2013; 238: 1047-1054.

108. The Effects of Aqueous Extract of Alpinia Galangal on Gastric Cancer Cells (AGS) and L929 Cells in Vitro / M.-A.-R. Hadjzadeh, H. Ghanbari, Z. Keshavarzi, J. Tavakol-Afshari // Iran. J. Cancer Prev. - 2014; 7: 142-146.

109. Halliwell, B. A super way to kill cancer cells? / B. Halliwell // Nature Medicine // 2000; 6 (10): 1105-1106.

110. Halliwell, B. Role of free radicals and catalytic metal ions in human disease: an overview / B. Halliwell, JM Gutteridge // Methods in Enzymology. - 1990; 186: 1–85.

111. Han, M. Quercetin suppresses the migration and invasion in human colon cancer Caco-2 cells through regulating toll-like receptor 4 / nuclear factor-kappa B pathway / M. Han, Y. Song, X. Zhang // Pharmacogn. Mag. - 2016; 12 (Suppl 2): 237-244.

112. Neurotransmitter metabolic enzymes and antioxidant status on Alzheimer ›s disease induced mice treated with Alpinia galanga (L.) / JC Hanish Singh, V. Alagarsamy, S. Sathesh Kumar, Y. Narsimha Reddy // Willd. Phytother Res. - 2011; 25: 1061-1067.

113. Flavonoids protect human retinal pigment epithelial cells from oxidative-stress-induced death / A. Hanneken, FF Lin, J. Johnson, P. Maher // Invest Ophthalmol Vis Sci. 2006; 47: 3164-3177.

114. Harirforoosh, S., Asghar W., Jamali F. Adverse effects of nonsteroidal antiinflammatory drugs: an update of gastrointestinal, cardiovascular and renal complications / S. Harirforoosh, W. Asghar, F. Jamali // J. Pharm Pharm Sci. 2014; 16: 821-847.

115. Hartwell, JL Plants Used Against Cancer: A Survey / JL Hartwell., Quarterman Publications, Inc., Lawrence, MA, 1982. (reprinted from 11 different issues of Lloydia)

116. Homeoden-Heel. Catalogus, Baden-Baden: Simile-Gent, 1998 .-- 204 p.

117. Homoopatihisches Arzneibuch. - 1. Ausgabe 1978. - Gesatausgabe. - Diese Gesamtausgabe nach der Neufassung 1985 enhalt die Teibande. HAB 1 1978, 1. Nachtrag 1981, 2. Nachtrag 1983, 3. Nachtrag 1985, 4. Nachtrag 1985. - Amtliche Ausgabe. - Deutscher Apotheker Verlag Stuttgart Govi - Verlag GmbH, Frankfurt. - 928 s.

118. Isolates of Alpinia officinarum Hance as COX-2 inhibitors: Evidence from anti-inflammatory, antioxidant

and molecular docking studies / VS Honmore, AD Kandhare, PP Kadam [et al.] // Int. Immunopharmacol. - 2016; 33: 8-17.

119. Protective effects of myricitrin against osteoporosis via reducing reactive oxygen species and bone-resorbing cytokines / Q. Huang, B. Gao, L. Wang [et al.] // Toxicol Appl Pharmacol. - 2014; 280: 550-560.

120. Ginsenoside-Rb2 displays anti-osteoporosis effects through reducing oxidative damage and bone-resorbing cytokines during osteogenesis / Q. Huang, B. Gao, Q. Jie [et al.] // Bone. 2014; 66: 306-314.

121.7- (4-Hydroxyphenyl) -1-phenyl-4E-hepten-3-one, a Diarylheptanoid from Alpinia officinarum, Protects Neurons against Amyloid-β Induced Toxicity / X. Huang, G. Tang, Y. Liao [et al.] // Biol. Pharm. Bull. - 2016. Vol. 39, No. 12. - R. 1961-1967.

122. Antimicrobial effect by extracts of rhizome of Alpinia officinarum Hance may relate to its inhibition of beta-ketoacyl-ACP reductase / H. Huang, D. Wu, WX Tian [et al.] // J. Enzyme. Inhib. Med. Chem. - 2008; 23: 362-368.

123. The natural flavonoid galangin inhibits osteoclastic bone destruction and osteoclastogenesis by suppressing NF-κB in collagen-induced arthritis and bone marrow-derived macrophages / JE Huh, IT Junq, J. Choi [et al.] // Eur J Pharmacol. 2013; 698: 57-66.

124. The effects of galangin on a mouse model of vitiligo induced by hydroquinone / SX Huo, XM Liu, CH Ge [et al.] // Phytother. Res. - 2014; 28: 1533-1538.

125. Essential oil composition and antimicrobial activities of two closely related species, Alpinia mutica Roxb. and Alpinia latilabris Ridl., from Peninsular Malaysia / H. Ibrahim, Y. Sivasothy, DR Syamsir [et al.] // Scientific World J. - 2014. - Vol. 2014: 430831.

126. Indian Council of Medical Research, Medicinal Plants of India, Vol. 1, Indian Council of Medical Research, Cambridge Printing Works, New Delhi, 1976.

127. Indian Council of Medical Research, Medicinal Plants of India, Vol. 2, Indian Council of Medical Research, Cambridge Printing Works, New Delhi, 1987.

128. Antitumour principles from Alpinia galangal / H. Itokawa, H. Morita, T. Sumitomo [et al.] // Planta Med. - 1987; 53: 32-33.

129. In vitro cytotoxicity of norviburtinal and isopinnatal from Kigelia pinnata against cancer cell lines / SJ Jackson, PJ Houghton, S. Retsas, A. Photiou // Planta Med. - 2000; 66: 758-761.

130. Ethacrynic acid analogs lacking the alpha, beta-unsaturated carbonyl unit - potential anti-metastatic drugs / RF Janser, RK Meka, ZE Bryant [et al.] // Bioorg. Med. Chem. Lett. - 2010; 20: 1848-1850.

131. Hydrogen peroxide-induced apoptosis in pc12 cells and the protective effect of puerarin / B. Jiang, -JH Liu, YM Bao, LJ An // Cell Biology International. - 2003; 27 (12): 1025-1031.

132. Anti-inflammatory effects of galangin on lipopolysaccharide-activated macrophages via ERK and NF-kappa B pathway regulation / YC Jung, ME Kim, JH Yoon [et al.] // Immunopharmacol. Immunotoxicol. - 2014; 36: 426-432.

133. Diarylheptanoids from Alpinia officinarum Cause Distinct but Overlapping Effects on the Translatome of B Lymphoblastoid Cells / T. Kakegawa, S. Takase, E. Masubuchi, K. Yasukawa // Evidence-Based Complementary and Alternative Medicine. - 2014; Vol. 2014: 204797–204797.

134. Elastase release by stimulated neutrophils inhibited by flavonoids: importance of the catechol group / A. Kanashiro, JC Souza, LM Kabeya [et al.] // Zeit Für Naturforschung. 2007. P.62: 357-361.

135. Osteoblastogenesis and osteoprotection enhanced by flavonolignan silibinin in osteoblasts and osteoclasts / JL Kim, SW Kang, MK Kang [et al.] // J Cell Biochem. 2012; 113: 247-259.

136. Localization and expression of inducible nitric oxide synthase in biopsies from patients with interstitial cystitis / LR Koskela, T. Thiel, I. Ehrén [et al.] // J. Urol. - 2008. –Vol. 180. - P.737-741.

137. LC – MS / MS analysis, antioxidant and anticholinergic properties of galanga (Alpinia officinarum Hance) rhizomes / LP Köse, İ. Gülçin, AC Gören [et al.] // Ind. Crops Prod. - 2015; 74: 712-721.

138. Kumar, S. Chemistry and biological activities of flavonoids: an overview / S. Kumar, AK Pandey // Scient. World J. - 2013; Vol. 2013: 162750.

139. Laine, L. Approaches to nonsteroidal anti-inflammatory drug use in the high-risk patient. Gastroenterology / L. Laine. - 2001; 120: 594-606.

140. Lanas A, Baron JA, Sandler RS, Horgan K, Bolognese J, Oxenius B, Quan H, Watson D, Cook TJ, Schoen R, et al. Peptic ulcer and bleeding events associated with rofecoxib in a 3-year colorectal adenoma chemoprevention trial. Gastroenterology. 2007. - 132: 490–497.

141. Effect of sesaminol glucosides on β-amyloid-induced PC12 cell death through antioxidant mechanisms / SY Lee, TY Ha, DJ Son [et al.] // Neuroscience Research. - 2005; 52 (4): 330-341.

142. Lee, CC Cytotoxicity of plants from Malaysia and Thailand used traditionally to treat cancer / CC Lee, P. Houghton // J. Ethnopharmacol. - 2005; 100: 237-243.

143. Screening of medicinal plant extracts for antioxidant activity / SE Lee, HJ Hwang, JS Ha [et al.] // Life Sci. - 2003; 73: 167-179.

144. Synergistic effects of the combination of galangin with gentamicin against methicillin-resistant Staphylococcus aureus / YS Lee, OH Kang, JG Choi [et al.] // J. Microbiol. –2008; 46: 283-288.

145. Anti-inflammatory, anti-nociceptive, and anti-psychiatric effects by the rhizomes of Alpinia officinarum on complete Freund's adjuvant-induced arthritis in rats / J. Lee, KA Kim, S. Jeong [et al.] // J. Ethnopharmacol. - 2009; 126: 258-264.

146. Effects of hydrogen peroxide (H2O2) on alkaline phosphatase activity and matrix mineralization of odontoblast and osteoblast cell lines / DH Lee, BS Lim, YK Lee, HC Yang // Cell Biol Toxicol. 2006; 22: 39–46.

147. Lesser Galangal - Alpinia officinarum // In book: PDR for Herbal Medicines (Physician ›s Desk Reference for Herbal Medicines); 4th Edition / by Thomson Healthcare (Author); published by Thomson Reuters, 2007 .-- 990 p. (R. 467-468).

148. Leung, PC Herbal treatment for osteoporosis: a current review / PC Leung, WS Siu // J Tradit Complment Med. 2013; 3: 82–87.

149. Li, BH Presence of fatty acid synthase inhibitors in the rhizome of Alpinia officinarum Hance / BH Li, W. Tian // J. Enzyme Inhib. Med. Chem. - 2003; 18: 349-356.

150. Lim TK Edible Medicinal and Non-Medicinal Plants: Modified Stems, Roots, Bulbs; Vol. 12 / TK Lim. - London: Springer, 2002 .-- P. 178.

151. Antihyperlipidemic bioactivity of Alpinia officinarum (Hance) Farw Zingiberaceae can be attributed to the coexistance of curcumin, polyphenolics, dietary fibers and phytosterols / LY Lin, CC Peng, XY Yeh [et al.] // Food Funct. - 2015; 6: 1600-1610.

152. List, PH Hager's Handbuch der Pharmazeutischen Praxis, Vols. 2-6. / PH List, L. Hohammer. - Springer-Verlag, Berlin, 1969-1979.

153. Liu, CN Antagonistic storage method of traditional Chinese medicinal material / CN Liu // J. Chin. Med. Mater. - 1987; 4: 36. - doi: 10.13863 / j.issn1001-4454.1987.04.022.

154. New cytotoxic diarylheptanoids from the rhizomes of Alpinia officinarum Hance / D. Liu, YW Liu, FQ Guan, JY Liang // Fitoterapia. - 2014; 96: 76-80.

155. A new dimeric diarylheptanoid from the rhizomes of Alpinia officinarum / D. Liu, W. Qu, L. Zhao [et al.] // Chin. J. Nat. Med. - 2014; 12: 139-141.

156. Dimeric Diarylheptanoids with Neuroprotective Activities from Rhizomes of Alpinia officinarum / H. Liu, X. Wang, Q. Shi [et al.] // ACS Omega. - 2020; 5 (17): 10167-10175. Published 2020 Apr 22.

157. Evaluation of Diarylheptanoid – Terpene Adduct Enantiomers from Alpinia officinarum for Neuroprotective Activities / H. Liu, Zh.-L. Wu, X.-J. Huang [et al.] // J. Natur. Prod. - 2018 .-- 81 (1).

158. Discrimination of Two Cultivars of Alpinia Officinarum Hance Using an Electronic Nose and Gas Chromatography-Mass Spectrometry Coupled with Chemometrics / Q. Long, Z. Li, B. Han [et al.] // Sensors (Basel, Switzerland). - 2019 Jan 30; 19 (3): 572.

159. Mechanism and inhibitory effect of galangin and its flavonoid mixture from Alpinia officinarum on mushroom tyrosinase and B16 murine melanoma cells / Lu YH, ZT Lin-Tao Wang, DZ Wei, HB Xiang // J. Enzyme Inhib. Med. Chem. - 2007; 22: 433-438.

160. Protective effect of galangin in Concanavalin A-induced hepatitis in mice / Q. Luo, L. Zhu, J. Ding [et al.] // Drug Des. Dev. Ther. - 2015; 9: 2983-2992.

161. Lü, J. Repellent and Contact Toxicity of Alpinia officinarum Rhizome Extract against Lasioderma serricorne Adults / J. Lü, D. Ma // PLoS One. - 2015; 10 (8): e0135631. - Published 2015 Aug 20.

162. Isolation and characterization of some antioxidative compounds from the rhizomes of smaller galangal (Alpinia officinarum Hance) / TN Ly, M. Shimoyamada, K. Kato, R. Yamauchi // J. Agricult. Food Chem. - 2003; 51 (17): 4924-4929.

163. Antioxidative compounds isolated from the rhizomes of smaller galangal (Alpinia officinarum Hance) / TN Ly, M. Shimoyamada, K. Kato, R. Yamauchi // Biofactors. - 2004; 21 (1-4): 305-308.

164. Isolation and structural elucidation of some glycosides from the rhizomes of smaller Galanga (Alpinia officinarum Hance) / TN Ly, R. Yamauchi, M. Shimoyamada, K. Kato, // J. Agricult. Food Chem. - 2002; 50 (17): 4919–4924.

165. Madaus, G., Lehrbuch der Biologischen Hilfmittel, Vol. 1-3 / G. Madaus. - Georg Olms Verlag, Hildescheim, 1976, reprint of 1938 Madaus

166. Malfertheiner, P. Peptic ulcer disease / P. Malfertheiner, FK Chan, KE Mccoll // Lancet. 2009. 374: 1449-1461.

167. Manolagas, SC From estrogen-centric to aging and oxidative stress: a revised perspective of the pathogenesis of osteoporosis / SC Manolagas // Endocr Rev. 2010; 31: 266-300.

168. Marx, RE Pamidronate (Aredia) and zoledronate (Zometa) induced avascular necrosis of the jaws: a growing epidemic / RE Marx // J Oral Maxillofac Surg. 2003; 61: 1115-1117.

169. Inhibitors from the rhizomes of Alpinia officinarum on production of nitric oxide in lipopolysaccharide-

activated macrophages and the structural requirements of diarylheptanoids for the activity / H. Matsuda, S. Ando, T. Kato T. [et al.] // Bioorg Med. Chem. - 2006; 14: 138-142.

170. Melanogenesis inhibitors from the rhizomes of Alpinia officinarum in B16 melanoma cells / Matsuda H., Nakashima S., Oda Y., Nakamura S., Yoshikawa M. // Bioorg Med. Chem. - 2009; 17: 6048-6053.

171. Mazzanti, G. Analgesic anti-inflammatory action of Pfaffia paniculata (martius) kuntze / G. Mazzanti, L. Braghiroli // Phytother. Res. - 1994; 8: 413-416.

172. American Herbal Products Association's Botanical Safety Handbook / M. McGuffin [et al.], Eds. - CRC Press, Boca Raton, FL, 1997.

173. Megahed, NA Antivirus-built environment: Lessons learned from Covid-19 pandemic / NA Megahed, EM Ghoneim // Sustain Cities Soc. - 2020 Oct; 61: 102350.

174.DissectingthePharmacophoreofCurcumin.WhichStructuralElementIsCritical forWhichAction? /A.Minassi,G. Sánchez-Duffhues, JA Collado [et al.] // J. Nat. Prod. - 2013; 76: 1105-1112.

175. Nitric oxide-mediated mechanism of neuronal nitric oxide synthase and inducible nitric oxide synthase expression during hypoxia in the cerebral cortex of newborn piglets / OP Mishra, R. Mishra, QM Ashraf, M. Delivoria-Papadopoulos // Neuroscience. - 2006. - Vol. 140. - P.857-863.

176. Reactive oxygen species in inflammation and tissue injury / M. Mittal, MR Siddiqui, K. Tran [et al.] // Antioxid Redox Signal. 2014; 20: 1126–67.

177. Chinese herbal medicine for bone health / E. Mukwaya, F. Xu, MS Wong, Y. Zhang // Pharm Biol. 2014; 52: 1223-1228.

178. Munnoli, PM Post-COVID-19 precautions based on lessons learned from past pandemics: a review / PM Munnoli, S. Nabapure, G. Yeshavanth // Z. Gesundh. Wiss. - 2020 Aug 4: 1-9.

179. Structure-activity relationships of (1-S ') - 1'-acetoxychavicol acetate, a major constituent of a Southeast Asian condiment plant Languas galangal on the inhibition of tumor-promoter-induced Epstein-Barr virus activation / Murakami A., Toyota K., Ohura S. [et al.] // J. Agric. Food. Chem. - 2000; 48: 1518-1523.

180. Ovariectomy induces oxidative stress and impairs bone antioxidant system in adult rats / S. Muthusami, I. Ramachandran, B. Muthusamy [et al.] // Clin Chim Acta. 2005; 360: 81–86. [PubMed] [Google Scholar]

181. A novel diarylheptanoid-bearing sesquiterpene moiety from the rhizomes of Alpinia officinarum / W. Na, ZL Zhou, Q. Wei [et al.] // Nat. Prod. Res. - 2016; 30: 2344-2349.

182. Extraction and identification of water soluble compounds in palm pressed fiber by SC-CO2and GC-MS / HL Nang, CY May, MA Ngan, CC Hock [et al.] // Am. J. Environ. Sci. - 2007; 3: 54-59.

183. The anti-inflammatory role of vitamin e in prevention of osteoporosis / AS Nazrun, M. Norazlina, M. Norliza, SI Nirwana // Adv Pharmacol Sci. 2012; 2012 Article ID 142702, 7 pages.

184. Nimse, SB Free radicals, natural antioxidants and their reaction mechanisms / SB Nimse, D. Pal // RSC Adv. - 2015; 5: 27986-8006. [Google Scholar]

185. Nrf2-Keap1 activation, a promising strategy in the prevention of cancer / OA Ojo, B. Ajiboye, A. Fadaka [et al.] // Frees Radic Antioxid. - 2017; 7: 1-7.

186. Antiproliferative activities of lesser galangal (Alpinia officinarum Hance), turmeric (Curcuma longa L.). and ginger (Zingiber officinale Rosc.) against acute monocytic leukemia / SN Omoregie, FO Omoruyi, VF Wright [et al.] // J. Med. Food. - 2013; 16: 647-55.

187. A guide to transient expression of membrane proteins in HEK-293 cells for functional characterization / A. Ooi, A. Wong, L. Esau [et al.] // Front Physiol. - 2016; 7: 300.

188. Role of flavonoids on oxidative stress and mineral contents in the retinoic acid-induced bone loss model of rat / N. Orsolic, E. Goluza, D. Dikic [et al.] // Eur J Nutr. 2014; 53: 1217-1227.

189. Parekh, J. Efficacy of aqueous and methanol extracts of some medicinal plants for potential antibacterial activity / J. Parekh, D. Jadeja, S. Chanda // Turk. J. Biol. - 2005; 29: 203-210.

190. Bisphosphonate use and the risk of subtrochanteric or femoral shaft fractures in older women / LY Park-Wyllie, MM Mamdani, DN Juurlink [et al.] // JAMA. 2011; 305: 783-789.

191. Pharmacopoeia of the People's Republic of China. Beijing: Chemical Industry Press / Editor: The State Pharmacopoeia Commission of the People's Republic of China. - Beijing: People's Medical Publishing House, 2005.

192. Pietta, PG Flavonoids as antioxidants / PG Pietta // J. Nat. Prod. - 2000; 63: 1035-42.

193. Therapeutic Potential of Alpinia officinarum / MK Pillai, DJ Young, Hj.A. Bin, HM Majid // Mini Rev Med Chem. - 2018; 18 (14): 1220-1232.

194. Polvani, S. PPARgamma and oxidative stress: Con (beta) catenating NRF2 and FOXO / S. Polvani, M. Tarocchi, A. Galli // PPAR Res. 2012; 2012 Article ID 641087, 15 pages.

195. Quoted in Strehlow Wighard, Hertzka Cottfried. Hildegard of Bingen's Medicine. - Inner Traditions, 1998. - P. 37.

196. Molecular basis of the anti-inflammatory potential of a diarylheptanoid in murine macrophage RAW 264.7 cells / BR Rajaganapathy, K. Thirugnanam, MV Shanmuganathan [et al.] // Adv. Biol. Chem. - 2013; 3: 541-548.

197. Antioxidant and anti-inflammatory activities of selected Chinese medicinal plants and their relation with antioxidant content / AS Ravipati, L. Zhang, SR Koyyalamudi [et al.] // BMC Complement. Altern. Med. - 2012; 12: 173.

198. Rawlings, M. The gene encoding Escherichia coli acyl carrier protein lies within a cluster of fatty acid biosynthetic genes / M. Rawlings M., JE Jr. Cronan // J. Biol. Chem. - 1992; 267: 5751-5754.

199. Reid K., Wright V., Omoregie S. Anticancer properties of Alpinia officinarum (lesser galangal) - A mini review // Int. J. Adv. Res. - 2016; 4: 300-306.

200. Oxidative stress, inflammation, and cancer: how are they linked? / S. Reuter, SC Gupta, MM Chaturvedi, BB Aggarwal // Free Radic Biol Med. 2010; 49: 1603-16.

201. Mitochondrial reactive oxygen species and inflammation: Molecular mechanisms, diseases and promising therapies / A. Rimessi, M. Previati, F. Nigro [et al.] // Int J Biochem Cell Biol. - 2016; 81 (Pt B): 281-293.

202. Adverse reactions and drug-drug interactions in the management of women with postmenopausal osteoporosis / R. Rizzoli, JY Reginster, S. Boonen [et al.] // Calcif Tissue Int. 2011; 89: 91-104.

203. Isosorbide 5 mononitrate administration increases nitric oxide blood levels and reduces proteinuria in IgA glomerulonephritis patients with abnormal urinary endothelin cyclic GMP ratio / D. Roccatello, G. Mengozzi, M. Ferro [et al.] // Clin. Nephrol. - 1995. - Vol. 44. - P.163-169.

204. Novel biomarkers in the diagnosis of chronic kidney disease and the prediction of its outcome / J. Rysz, AID Gluba-Brzózka, B. Franczyk [et al.] // Int. J. Mol. Sci. - 2017; 18: 1702.

205. Sak, K. Sak, K. Cytotoxicity of dietary flavonoids on different human cancer types, Pharmacogn. Rev. - 2014; 8: 122-146.

206. Quercitrin and taxifolin stimulate osteoblast differentiation in MC3T3-E1 cells and inhibit osteoclastogenesis in RAW 264.7 cells / M. Satue, M. Arriero Mdel, M. Monjo, JM Ramis // Biochem Pharmacol. 2013; 86: 1476-1486.

207. Shahid Akbar. Handbook of 200 Medicinal Plants: A Comprehensive Review of Their Traditional Medical Uses and Scientific Justifications / Akbar Shahid. - Springer Nature Switzerland AG 2020. - 2020. - P. 217-224.

208. Effects of the hook of Uncaria rhynchophylla on neurotoxicity in the 6-hydroxydopamine model of Parkinson's disease / JS Shim, HG Kim, MS Ju [et al.] // J. Ethnopharmacology. - 2009; 126 (2): 361–365.

209. Galangin dampens mice lipopolysaccharide-induced acute lung injury / YS Shu, W. Tao, QB Miao [et al.] // Inflammation. 2014; 37: 1661-1668.

210. Sivakumar, AS Effect of galangin supplementation on oxidative damage and inflammatory changes in fructose-fed rat liver / AS Sivakumar, CV Anuradha // Chem Biol Interact. - 2011.193: 141-148.

211. Sivakumar, AS Dose-dependent effect of galangin on fructose-mediated insulin resistance and oxidative events in rat kidney / AS Sivakumar, P. Viswanathan, CV Anuradha // Redox Rep. - 2010; 15: 224-232.

212. Smith, MB Advanced Organic Chemistry: Reactions, Mechanisms and Structure; 6th ed. / MB Smith, J. March. - New York: Wiley-Interscience, 2007.

213. Sostres, C. Nonsteroidal anti-inflammatory drugs and upper and lower gastrointestinal mucosal damage / C. Sostres, CJ Gargallo, A. Lanas // Arthritis Res Ther. - 2013.15: S3.

214. Spencer, JP The interactions of flavonoids within neuronal signaling pathways / JP Spencer // Genes Nutr. - 2007; 2: 257-273.

215. Antioxidant and antimicrobial activity of Alpinia officinarum / AR Srividya, SP Dhanabal, VK Misra, G. Suja // Indian J. Pharm. Sci. - 2010; 72: 145-148.

216. Steinmetz, EF Codex Vegetabilis. All Botanical Drugs / EF Steinmetz. - Keizersgracht 347, Amsterdam, 1957.

217. Case-control study of postmenopausal hormone replacement therapy and endometrial cancer / BL Strom, R. Schinnar, AL Weber [et al.] // Am J Epidemiol. - 2006; 164: 775-786.

218. Antiosteoporotic effects of Alpinia officinarum Hance through stimulation of osteoblasts associated with antioxidant effects / Y. Su, Y. Chen, Y. Liu [et al.] // J. Orthop. Translat. - 2015 Oct 29; 4: 75-91.

219. Protective effect of albiflorin against oxidative-stress-mediated toxicity in osteoblast-like MC3T3-E1 cells / KS Suh, EM Choi, YS Lee, YS Kim // Fitoterapia. - 2013; 89: 33–41.

220. Suja, S. Inhibition of in vitro cytotoxic effect evoked by Alpinia galanga and Alpinia officinarum on PC - 3 cell line / S. Suja, P. Chinnaswamy // Anc. Sci. Life. - 2008; 27: 33-40.

221. Sultana, B. Effect of extraction solvent / technique on the antioxidant activity of selected medicinal plant extracts / B. Sultana, F. Anwar, M. Ashraf // Molecules. - 2009; 14: 2167-2180.

222. New cytotoxic diarylheptanoids from the rhizomes of Alpinia officinarum / Y. Sun, K. Tabata, H. Matsubara [et al.] // Planta Medica. - 2008; 74 (4): 427-431.

223. Diarylheptanoids derived from Alpinia officinarum induce apoptosis, S-phase arrest and differentiation in human neuroblastoma cells / K. Tabata, Y. Yamazaki, M. Okada [et al.] // Anticancer Res. - 2009; 29: 4981-4988.

224. Identification of chemical constituents occurring in leaves of Alpinia officinarum / YF Tan, HL Li, YB Li [et al.] // Chin. J. Exp. Tradit. Med. Formula. - 2015; 3: 37-40.

225. A natural diarylheptanoid promotes neuronal differentiation via activating ERK and PI3K-Akt dependent pathways / G. Tang, X. Dong, X. Huang [et al.] // Neuroscience. - 2015. - Vol. 303. - P. 389-401.

226. Tschirch A. Handbuch der Pharmakognosie [A handbook of pharmacognosy]. - Leipzig: Verlag CH Tauchnitz, 1923.

227. Turner, J. Spice: The history of a Temptation / J. Turner. - US: Vintage (2005). - P.195; Knopf doubleday Publishing Group, 2008 .-- 384 p.

228. Evaluation of cytotoxic and mutagenic effects of coriolus versicolor and Funalia trogii extracts on mammalian cells / A. Ünyayar, M. Demirbilek, M. Turkoglu [et al.] // Drug. Chem. Toxicol. - 2006; 29 (1): 69–83.

229. Urquiza-Martinez, MV Antioxidant capacity of food / MV Urquiza-Martinez, BF Navarro // Free Radic Antioxid. - 2016; 6: 1-12.

230. Chemical composition of the fractions of leaf oil of Alpinia zerumbet (Pers.) BL Burtt & RM Sm. and antimicrobial activity / CP Victório, DS Alviano, CS Alviano, CLS Lage // Brazilian. J. Pharmacognosy. - 2009; 19 (3): 697-701.

231. Research on Alpinia officinarum Hance oil against experimental gastrelcosis and action mechanism / H.-Y. Wang, Ya-M. Liu, H.-Y. Li [et al.].

232. Watt, G. Dictionary of the Economic Products of India, 6 vols. / G. Watt. - Nav Bharat Offset Process, Delhi, India, 1889-1892, reprint 1972.

233. Effect of different extraction parts of galangal on experimental gastric ulcer / N. Wei, YF Tan, F. Chen // J. Hainan Med Univ. 2015. - 21: 158-160. http://scholar.google.com/scholar_lookup?hl=en & volume = 21 & publication_year = 2015 & pages = 158-160 & author = N + Wei & author = YF + Tan & author = F + Chen & & author = H + Li & author = JQ. + Zhang title = Effect + of + different + extraction + parts + of + galangal + on + experimental + gastric + ulcer

234. Anovel diarylheptanoid-bearing sesquiterpene moiety from the rhizomes of Alpinia officinarum / N. Wei, Z. Zhou, Q. Wei [et al.] // Nat. Prod. Res. –2016; 30: 2344-2349.

235. Wen, YY A new diterpenoid from Alpinia Zerumbet / YY Wen, YF Chen, XM Xie // Acta Botanica Sinica. - 1997; 399 (10): 983-984.

236. Two anti-inflammatory diterpenes from the rhizomes of Alpinia officinarum Hance / T. Wen, XK Wang, C. Liu, H. Liu // J. Pharm. Biomed. Sci. - 2016; 6: 479-482.

237. Wickens, AP Aging and the free radical theory / AP Wickens // Respiration Physiology. - 2001; 128 (3): 379-391.

238. Wijayaratne, LKW Methoprene and control of stored-product insects / LKW Wijayaratne, FH Arthur, S. Whyard // J. Stored. Prod. Res. 2016. - Vol. 76.

239. Williamson, EM Potter's New Cyclopaedia of Botanical Drugs and Preparations, revised ed. / EM Williamson and FJ Evans. - Saffron Walden, the CW Daniel Co., Ltd., Essex, UK, 1988, reprint 1989.

240. Wolfe, MM Gastrointestinal toxicity of nonsteroidal antiinflammatory drugs / MM Wolfe, DR Lichtenstein, G. Singh // New Engl. J. Med. - 1999; 340: 1888-1899.

241.7- (4-Hydroxy-3-methoxyphenyl) -1-phenyl-4E-hepten-3-one alleviates Aβ1-42 induced cytotoxicity through PI3K-mTOR pathways / HL Xiao, QH Zhang, YH Peng [et al.] // Biochemical and biophysical research communications. - 2017. - Vol. 484. - No. 2. - P.365–371.

242. Antibacterial activities of flavonoids: structure-activity relationship and mechanism / Xie Y., W. Yang, F. Tang [et al.] // Curr. Med. Chem. - 2015; 22: 132-149.

243. Chemical Constituents of Supercritical Extracts from Alpinia officinarum and the Feeding Deterrent Activity against Tribolium castaneum / M. Xin, S. Guo, W. Zhang [et al.] // Molecules (Basel, Switzerland). - 2017 .-- 22 (4): 647.

244. Epimedium-derived flavonoids modulate the balance between osteogenic differentiation and adipogenic differentiation in bone marrow stromal cells of ovariectomised rats via Wnt / β-catenin signal pathway activation / YX Xu, CL Wu, Y. Wu [et al.] // Chin J Integr Med. 2012; 18: 909-917.

245. Yadav, PN diarylheptanoid from lesser galangal (Alpinia officinarum) inhibits pro-inflammatory mediators viainhibition of mitogen-activated protein kinase, p44 / 42, and transcription factor nuclear factor-kappa B / PN Yadav, Z. Liu, MM Rafi // J. Pharmacol. Exp. Ther. - 2003; 305: 925-931.

246. Organic acids and water-soluble phenolics produced by Paxillus sp 60/92 together show antifungal activity against Pythium vexans under acidic culture conditions / K. Yamaji, H. Ishimoto, N. Usui, S. Mori // Mycorrhiza. - 2005; 15: 17-23.

247. Tanshinol attenuates the deleterious effects of oxidative stress on osteoblastic differentiation via Wnt / FoxO3a signaling / YJ Yang, YJ Su, D. Wang [et al.] // Oxid Med Cell Longev. 2013; 2013 Article ID 351895, 18 pages.

248. Yang, RZ Plants used for pest control in China: a literature review / RZ Yang, CS Tang // Econ. Bot. - 1988; 42: 376-406.

249. Motohashi S. Inhibitory effect of the rhizomes of Alpinia officinarum on TPA-induced inflammation and

tumor promotion in two-stage carcinogenesis in mouse skin / K. Yasukawa, Y. Sun, S. Kitanaka [et al.] // J. Nat. Med. - 2008; 62: 374-378.

250. Analysis of active constituents of Alpinia officinarum Hance from different localities of Hainan province / HL Zhai, Q. Li, H. Wang [et al.] // J. Trop. Biol. - 2014; 2: 188-193.

251. Three new antibacterial active diarylheptanoids from Alpinia officinarum / BB Zhang, Y. Dai, ZX Liao, LS Ding // Fitoterapia. - 2010; 81: 948-952. - doi: 10.1016 / j.fitote.2010.06.015

252. Galangin induces B16F10 melanoma cell apoptosis via mitochondrial pathway and sustained activation of p38 MAPK / W. Zhang, Y. Lan, Q. Huang, Z. Hua // Cytotechnology. - 2013; 65: 447-455.

253. Zhang, W.-J. The Genus Alpinia: A Review of Its Phytochemistry and Pharmacology / W.-J. Zhang, J.-G. Luo, L.-Y. Kong // World J Tradit Chin Med 2016; 2 (1): 26–41.

254. Simultaneous quantification of seventeen bioactive components in rhizome and aerial parts of Alpinia officinarum Hance using LC-MS / MS / JQ Zhang, Y. Wang, HL Li [et al.] // Anal. Methods. - 2015; 7: 4919.

255. Galangin induces apoptosis in hepatocellular carcinoma cells through the caspase 8 / t-Bid mitochondrial pathway / HT Zhang, J. Wu, M. Wen [et al.] // J. Asian Nat. Prod. Res. - 2012; 14: 626-33.

256. Flavonoids from the Aerial Parts of Alpinia officinarum / H. Zhang, LX Xu, P. Wu, XY Wei // J. Trop. Subtrop. Bot. - 2014; 22: 89-92.

257. Zhu, JX Progress on Alpinia officinarum Hance / JX Zhu, W. He, JC Ma // Food Drug. - 2009; eleven: 68-70.

258. Galangin inhibits growth of human head and neck squamous carcinoma cells in vitro and in vivo / L. Zhu, Q. Luo, J. Bi [et al.] // Chem. Biol. Interact. - 2014; 224: 149-156.

259. A new labdane diterpene from the rhizomes of Alpinia officinarum / QY Zou, HF Wu, YL Tang, DZ Chen // Nat. Prod. Res. - 2016; 30: 1-6.

Author's address

D.Pharm.Sci. Kiseleva T.L., professor,

Director of the Scientific Research Center-President of the NO "Professional Association of Naturotherapists".

kiselevaTL@yandex.ru

Kiseleva, T.L. Alpinia officinalis (Alpinia officinarum). Publication 3: biological action, application in traditional medicine and modern world medico-pharmaceutical practice / T.L. Kiseleva // Traditional medicine. - 2020. - No. 4 (63). - S.15-46.

To favorites