ANTICANCER AND ANTIOXIDANT POTENTIAL OF THE FRUITS OF VACCINIUM VITIS-IDAEA L. AND PROSPECTS FOR THEIR USE IN THE PREVENTION OF BREAST CANCER

D.G. Tikhonov[1], *K.M. Stepanov*[2*], *R.N. Zakharova*[1]

[1] North Eastern Federal University, Medical Institute, 58 Belinskogo St., Yakutsk, 677000, Russia;
2 Federal Research Centre FSBEI HE Arctic SATU, "The Yakut Scientific Centre of the Siberian Branch of the Russian Academy of Sciences", Sergelyakhskoe sh. 3 km, Yakutsk, 677000, Russia.

* Corresponding author: stenko07@mail.ru

Abstract. A review using the information on the problem in domestic and foreign sources of literature was carried out. Selected wild berries of Yakutia in their composition contain anthocyanins, flavanols and other biologically active compounds with experimentally proven anticancer effect in vitro against breast cancer cells. It has been noted that there is an insufficient study of wild berries as preventive agents against breast cancer. Experimental studies have proven the role of lingonberry in inhibiting the development of carcinogen-induced epithelial cancer, and cell culture of lingonberry and cloudberry can reduce the viability and proliferative activity of breast cancer cells. It is recommended to conduct researches on the effect of extracts, juice of northern berries on the development of breast cancer cell culture and find out their possible preventive and therapeutic effect.

Keywords: wild berries, lingonberries, chemical composition, antioxidant potential, anticancer potential, breast cancer, preventive means.

List of Abbreviations
BC – breast cancer

Introduction

Currently, a large number of biologically active compounds of plant origin with antitumor activity is identified, but a significant class of these compounds: essential oils, acids, alkaloids, flavonoids, styrene's, etc. until now are not widely used in the treatment and prevention of malignant tumors. Wild berries, which are massively harvested by the population for preservation, are of particular interest: lingonberry (*Vaccinium vitis-idaea L.*), blueberry (*Vaccinium uliginosum L.*), red currant (*Ribes rubrum L.*), black currant (*Ribes nigrum L.*), cloudberry (*Rubus chamaemorus*). All of them contain anthocyanins, flavanols and other biologically active compounds with experimentally proven anticancer effects in vitro against breast cancer (BC) cells. The most massively consumed berry in Yakutia is lingonberry. We paid attention to this berry when studying the incidence of BC in Yakutia. Consumption of fruits and vegetables is a generally recognized protective factor, and red meat is a risk factor (Poorolajal *et al.*, 2021). The population of Yakutia (especially the indigenous population) traditionally consumes little fruit and vegetables, but cannot do without red meat, but nevertheless age-standardized studies of BC incidence showed a very low level, not only at the level of Russia, but also relative to world indicators. It is known that lingonberry is a berry traditionally consumed in large quantities by the population of Yakutia. In this work we tried to draw public attention to lingonberry as a protective factor for BC. Unfortunately, up to the present time not only anticancer effects of fractions of this wild local berry have been insufficiently studied but also the role of lingonberry on BC risk in the northern conditions has been extremely insufficiently studied.

The purpose of the study is to review the studies conducted around the world and to draw attention to the gap in research on the role of lingonberry in the prevention of breast cancer.

Material and Methods

The search was performed in the Pubmed and eLibrary databases with the search queries «lingonberry and breast cancer», «lingonberry and breast cancer», «*Vaccinium vitis-idaea L.* and breast cancer», «брусника and «рак молочной железы» with no search term limit. An additional search was conducted with the query ««Wild Berries» and Breast Cancer Prevention». Articles were also searched by reference to literary sources.

doi: 10.24412/2500-2295-2023-1-58-71

Results

Lingonberry is the most common wild berry in the Russian Far East. Thus, its average annual biological reserves in this territory are 610 thousand tons (crude weight) (Korovkova, 2017), and according to the estimated data of the Institute of Cryolithozone Biology of the Siberian Branch of the Russian Academy of Sciences only in Yakutia the total resource reserve of lingonberry is 2.1 million tons (Nechaev, 2018). According to the calculations of A.P. Isayev, the total biological stock of lingonberry on the territory of Yakutia is estimated to be 23.6 thousand tons, and the total exploitable stock is 12.6 thousand tons (Isaev, 2021). It should be noted that lingonberries harvested by different farms for production needs from 37.5 to 59.3 tons per year are purchased on the territory of the region (Malysheva & Samsonova, 2022). Our calculations based on the data of V. Seroshevsky, the Yakuts at the end of the 19th century consumed on average 9.0 g of lingonberries per person per day (Tikhonov *et al.*, 2019). Yakut ethnographer of the early 20th century A.A. Savvin wrote: «In Central Yakutia, in places where the dominant branch of economy was cattle breeding, berries, along with wild plants, in the diet of the population played a significant role as dressing to various types of dairy products. They were stocked for the winter in almost all households. In the uluses (districts) of the Yakut region most households stocked 30-80 kg of lingonberries" (Savvin, 2005). Unfortunately, there is no exact data on how much lingonberry is currently harvested by the population of Yakutia for personal consumption, but it should be noted that until now the rural population uses lingonberry daily as part of the traditional breakfast Kyurchekh (whipped cream). According to the survey of respondents from 6 districts of Yakutia, 56.3% of the respondents prefer to consume products derived from wild berries in winter time daily (Petrova, 2018).

Chemical composition of *Vaccinium vitis-idaea L.* Lingonberries contain a wide range of biologically active compounds useful for health (Rasouli *et al.*, 2017), which allowed a number of researchers to classify it as a «super berry». (Kowalska, 2021; Mane *et al.*, 2011). It is particularly rich in polyphenolic compounds. They are usually called a diverse group of compounds found in food products of plant origin. Polyphenols are compounds that have more than one phenolic hydroxyl group attached to one or more benzene rings (Vermerris & Nicholson, 2009). Classification of polyphenolic compounds is a difficult task due to the fact that these compounds include a wide variety of phytochemical compounds (Prabhu *et al.*, 2021; Quideau *et al.*, 2011; Rasouli *et al.*, 2017) and, therefore, a number of researchers distinguish them into only two groups: flavonoids and non-flavonoids (Corcoran *et al.*, 2012). Jin Biao, Department of Chemistry, Jiangxi University of Science and Technology, Ganzhou, China categorizes food polyphenols into four main groups: phenolic acids, flavonoids, stilbenes and lignans (Jin, 2022). These compounds are secondary metabolites of higher plants and are usually involved in pollinator recruitment, protection against ultraviolet (UV) radiation, microbes and viruses, and herbivory (Cutrim & Cortez, 2018). Phenolic acids are subdivided into derivatives of benzoic (hydroxybenzoic, vanillic, protocatech, gallic and ellagic) and cinnamic (hydroxycinnamic, caffeic, alpha-cyano-4-hydroxycinnamic, ferulic, coumaric, synapic) acids (Prabhu *et al.*, 2021). High levels of benzoic acid are noted in Vaccinium berries (cranberries, lingonberries, blueberries) from 300-1300 mg per kg of fruit (Wibbertmann *et al.*, 2005). Numerous representatives of phenolic acids have a wide biological effect on the human body in its use (Kumar & Goel, 2019). Flavonoids are the most numerous groups of polyphenolic compounds. Most flavonoids are present in the form of 3-O-glycosides, except flavonols. Currently, the number of unique flavonoids identified exceeds 5000 compounds (Corcoran *et al.*, 2012). Flavonoids are divided into 6 main subclasses: Flavan-3-ols, Flavanones, Flavones, Isoflavones, Flavonols, Anthocyanins (Cazarolli *et al.*, 2008; Corcoran *et al.*, 2012; Shen *et al.*, 2022). Stilbenes are a class of phenolic secondary metabolites of plant origin, characterized by the presence of 1,2-diphenylethylene core and are of significant interest due to their medicinal properties. The best-known stilbene is resveratrol (Ren *et al.*, 2021). Lignin is one of the main components of the plant cell wall and is a natural phenolic polymer with a high molecular weight, complex composition and structure. In the biosphere, this polymer occupies 30% of the organic carbon (Liu *et al.*, 2018). The total content of phenolic compounds in the cranberry water-alcohol extracts ranged from 468.0 ± 10.1 to 661.1 ± 22.4 mg GAE / 100 g FW (fresh weight, GAE - gallic acid equivalent) (Dróżdż *et al.*, 2017; Lyutikova & Botirov, 2015).

Lingonberry samples from Alaska had phenolic compounds of 624.4 mg/100 g FW (Grace *et al.*, 2014). Lingonberry contains three major anthocyanins: cyanidin-3-galactoside (79%), cyanidin-3-glucoside (10%), and cyanidin-3-arabinoside (11%); its total content in cultivated lingonberry cultivars from Oregon was 27.4 to 51.6 mg/100 g FW (Lee &

Finn, 2012). Relatively high levels of anthocyanins are found in wild lingonberries from Scandinavian countries: 174 mg/100g FW (Andersen, 1985), 130.3 mg/100g FW (Määttä-Riihinen *et al.*, 2004). The most biologically active components of the chemical composition of lingonberry are shown in Table 1.

Table 1

The most biologically active components of the chemical composition of *Vaccinium vitis-idaea L.*

Lingonberry components	Content mg/ 100 g FW
Polyphenolic compounds	
Polyphenols	480.0 mg (Volkova *et al.*, 2018)
Total phenolicc	378.6 mg (Wang *et al.*, 2005)
Acid composition	
Ursolic acid	750 mg (Lyutikova & Botirov, 2015)
Benzoic acid	100.9–141.3 mg (Lyutikova, 2013)
Chlorogenic acid	2,3 mg (Bystrova & Alekseenko, 2017)
Chlorogenic acid *	3.5 mg (Bystrova & Alekseenko, 2017)
Cinnamic acid	1.39 – 3.65 mg (Lyutikova, 2013)
Coumaric acid	1.08 – 4.38 mg (Lyutikova, 2013)
Ferulic acid	0.16 – 0.98 mg (Lyutikova, 2013)
Terpene compounds	
D-limonen	0.51 – 1.77 mg (Lyutikova, 2013)
Oleanolic acid	209.3 – 214.8 mg (Szakiel *et al.*, 2012)
Ursolic acid	604.0 – 676.4 mg (Szakiel *et al.*, 2012)
sum of triterpene acids	813.3 – 891.2 mg (Szakiel *et al.*, 2012)
Flavonoids	
Flavonoids total	11.46 mg (Bystrova & Alekseenko, 2017)
Flavan-3-ols	
(+)-Catechin	152.7 – 243.6 mg (Liu *et al.*, 2020)
(-)-Epicatechin	34.1 – 38.6 mg (Liu *et al.*, 2020)
Flavonols	
Quercetin-3-O-galactoside	35.5 – 58.8 mg (Liu *et al.*, 2020)
Quercetin-3-O-rhamnoside	36.5 – 46.1 mg (Liu *et al.*, 2020)
Anthocyanidins	
Anthocyanin*	45.4 mg (Wang *et al.*, 2005)
Cyanidin-3-O-galactoside	238.9 – 308.4 mg (Liu *et al.*, 2020)
Cyanidin-3-O-glucoside	17.1 – 21.1 mg (Liu *et al.*, 2020)
Cyanidin-3-O-arabinoside	49.8 – 75.3 mg (Liu *et al.*, 2020)
Delphinidin-3-O-galactoside**	3.41 mg (Vilkickyte & Raudone, 2021)
Petunidin-3-O-glucoside**	1.61 mg (Vilkickyte & Raudone, 2021)
Peonidin-3-O-glucoside**	3.12 mg (Vilkickyte & Raudone, 2021)
Plant steroids	
Campesterol	10.1 – 15.2 mg (Szakiel *et al.*, 2012)
Sitosterol	132.8 – 135.7 mg (Szakiel *et al.*, 2012)
Stigmastadienone	9.7 – 24.5 mg (Szakiel *et al.*, 2012)
Stigmasterol	5.9 – 6.5 mg (Szakiel *et al.*, 2012)
sum of steroids	159.1 – 181.4 (Szakiel *et al.*, 2012)
Procyanidins	
sum of A-type Procyanidin dimers (m/z 575)	8.05 – 9.75 mg (Jungfer *et al.*, 2012)
sum of A-type Procyanidin trimers (m/z 863)	7.69 – 10.01 mg (Jungfer *et al.*, 2012)
Stilbens	

End of table 1

Lingonberry components	Content mg/ 100 g FW
Trans-resveratrol	3.0 mg (Ehala *et al.*, 2005)
Pectins etc	
Pectin substances	0.70 mg (Volkova *et al.*, 2018)
Vitamin C	24.2 – 31.9 mg (Lyutikova, 2013)

Note: * Lingonberry juice; ** October, these anthocyanidins appear in berries in late autumn

Discussion

Does nutrition have an effect on the risk of BC? A systematic review of 47 second level studies, meta-analyses, and literature reviews concluded that consumption of vegetables, fruits, and mushrooms are inversely related to BC. The same association has been noted with the intake of certain nutrients: calcium, folic acid, vitamin D, lignans, and carotenoids (Buja *et al.*, 2020). It is thought that a number of dietary characteristics can be risk factors for BC: heme iron intake and high serum iron levels (Chang *et al.*, 2019), frequent consumption of processed meat (Farvid *et al.*, 2018), Western diet (Xiao *et al.*, 2019), decreased serum zinc concentrations (Jouybari *et al.*, 2019), alcohol intake, red meat (Chen *et al.*, 2014) and vitamin D deficiency (Hossain *et al.*, 2019). At the same time, folic acid (Chen *et al.*, 2014), supplemental intake of vitamin D (Hossain *et al.*, 2019), a diet that includes vegetables and limits saturated fat, red meat and processed meat, can reduce the risk of developing BC (Dandamudi *et al.*, 2018). It should be noted that Giuseppe Grosso et al. from leading cancer research centers in Italy, the UK and the USA state that the evidence for the effect of diet on breast cancer is not conclusive and may be due to or mediated by lifestyle factors (Grosso *et al.*, 2017).

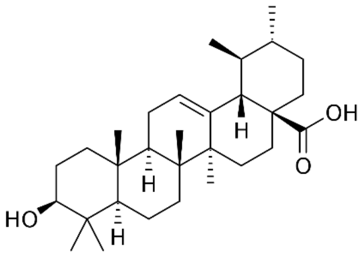
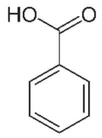
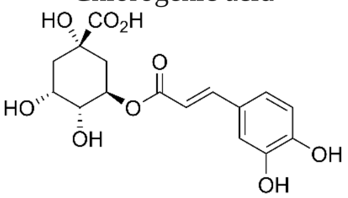
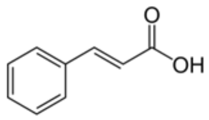
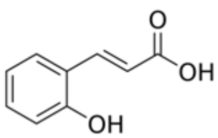
It is thought that a diet rich in fruits and vegetables may reduce the risk of BC due to polyphenols. It should be noted that lingonberry with its high level of polyphenols has multiple positive effects on human health (Kowalska, 2021). Lingonberry differs from other berries in its high level of antioxidant activity (Bujor *et al.*, 2018; Dróżdż *et al.*, 2017; Heinonen, 2007; Kostka *et al.*, 2022; Vilkickyte *et al.*, 2022; Vilkickyte *et al.*, 2020; Wang *et al.*, 2005). The main sources of reactive oxygen species in the organism are: mitochondrial respiratory chain, UV radiation, chemical oxidants, lipid/purine metabolism, physiological production of reactive oxygen species (ROS) and oxidative protein folding (Karbyshev & Abdullaev, 2018; Chesnokova *et al.*, 2006). Free radicals are ROS that are produced in the body during respiration. Free radicals (FR) cause chain reactions in cell membranes, disrupting their structures. Three basic forms of FR are known: hydroxyl radical, the most reactive and unstable chemical compound, which attacks any cell structure without selectivity, it can cause oxidative modification of nucleic acids; hydrogen peroxide can penetrate into the cell nucleus and transform into hydroxyl radical in the presence of iron; superoxide radical is formed mainly in mitochondria as a result of electron leakage during electron transport along the electron transfer chain (Lysenko, 2021; Martusevich & Karuzin, 2015; Tikhonov *et al.*, 2022). Antioxidants prevent free radical oxidation by reducing and binding free radicals. Studies have shown that lingonberry leaves and fruits possess not only antioxidant properties, but also antimicrobial (Viljanen *et al.*, 2014), antiviral (Mattio *et al.*, 2020; Nikolaeva-Glomb *et al.*, 2014), antifungal activity (Ermis *et al.*, 2015), protect against heart disease (Isaak *et al.*, 2015) obesity (Ryyti *et al.*, 2020), have hypolipidemic (Olennikov *et al.*, 2022), anti-inflammatory (Kivimäki *et al.*, 2014; Kowalska *et al.*, 2019), neuroprotective effect (Kelly *et al.*, 2018) and antimutagenic, anticancer activity (Lang *et al.*, 2011; Martinez-Perez *et al.*, 2014).

Various components of the chemical composition of lingonberry are known to have antitumor activity against BC in isolation. One of the most promising in this respect is ursolic acid, which is contained in cranberries up to 750 mg per 100 g of fresh berries (see Table 2).

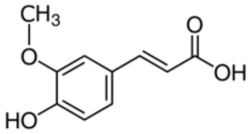
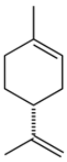
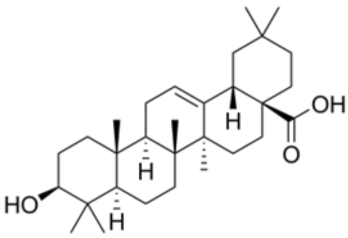
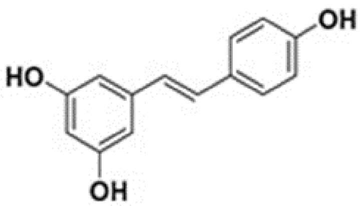
Thus, ursolic acid inhibits the growth of breast cancer cells in vitro by inhibiting proliferation, inducing autophagy, apoptosis and suppressing inflammatory reactions (Kim, 2021; Luo *et al.*, 2017), and also suppresses metastasis of BC (Wang *et al.*, 2021). According to a number of researchers, benzoic acid derivatives are potential antitumor agents with clinical prospects for breast cancer therapy (Lee *et al.*, 2014). A potential candidate for breast cancer therapy is chlorogenic acid (Changizi *et al.*, 2021; Zeng *et al.*, 2021), which is found in small amounts in cranberries. Clinical trials have shown that a representative of monoterpenes D-limonene

Table 2

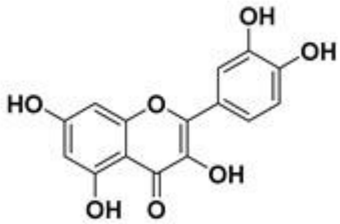
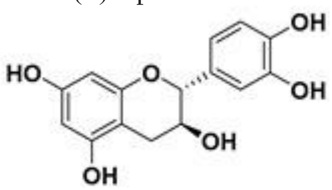
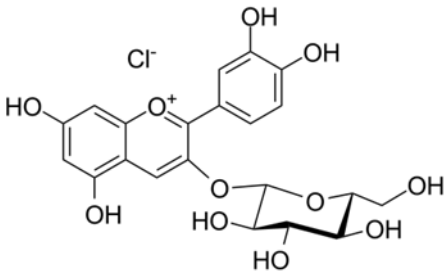
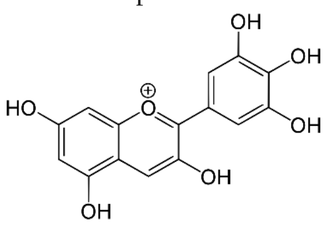
Summary of various biologically active compounds of lingonberries, their chemical structures, and breast anticancer effects

Biologically active compounds	**Applications in Breast Cancer Therapy and mechanism of action**	**Experimental studies *in vitro*, *in vivo*. References**
Ursolic acid 	Ursolic acid inhibits breast cancer growth by inhibiting proliferation, inducing autophagy and apoptosis, and suppressing inflammatory responses via the PI3K/AKT and NF-κB signaling pathways in vitro. Inhibits the metastasis of breast cancer by suppressing glycolytic metabolism through the activation of SP1/caveolin-1 signaling.	(Kim, 2021; Luo *et al.*, 2017; Wang *et al.*, 2021)
Benzoic acid 	Benzoic acid significantly suppresses the viability of breast cancer cells MCF-7, MDA-MB-468. It exhibits antitumor activity by stopping the cell cycle during the G_2/M phase and causing apoptosis in breast cancer cells. Increases the activity of caspase-3.	(Lee *et al.*, 2014)
Chlorogenic acid 	Chlorogenic acid (CA) in the model of invasive breast cancer in BALB/c mice statistically significantly reduced metastatic nodes compared to the control and eliminated the tumor at the end of the experiment. CA induces apoptosis of cancer cells and affects apoptotic agents: it significantly increases the Bax/Bcl-2 ratio and increases p53 gene expression compared to the control group. By disrupting the NF-kb/EMT signaling pathways, it improves anti-tumor immunity by providing anti-tumor and anti-metastatic effects.	(Changizi *et al.*, 2021; Zeng *et al.*, 2021)
Cinnamic acid 	Cinnamic acid is an effective anticancer agent that can induce apoptosis in breast cancer cells via TNFA-TNFR1 mediated extrinsic apoptotic pathway.	(Pal *et al.*, 2021)
o-Coumaric acid 	o-Coumaric acid exhibits anticarcinogenic effects by stimulating various pathways, including apoptosis, cell cycle regulation, and tumor suppression. It can stimulate the metabolic breakdown of toxic chemicals metabolized by CYP2E1 and CYP1A2 through increased expression of these isoenzymes, while coumaric acid inhibits the CIP3A4	(Sen *et al.*, 2013)

Continuation of the table 2

Biologically active compounds	**Applications in Breast Cancer Therapy and mechanism of action**	**Experimental studies *in vitro*, *in vivo*. References**
	isoenzyme, which may reduce the level of inactivation of drugs metabolized by this isoenzyme.	
Ferulic acid 	Treatment with ferulic acid (FA) results in decreased viability, increased apoptosis, and suppressed metastatic potential in the MDA-MB-231 breast cancer cell line. The antitumor activity of FA and its role in the suppression of metastasis are regulated by the reverse epithelial-mesenchymal transition (EMT). Because FA is a natural antioxidant that is poorly soluble in water, it is most promising to include it in a cyclodextrin nanosponges to increase cytotoxicity and deliver it to the lesions.	(Rezaei *et al.*, 2019; Zhang *et al.*, 2016)
D-limonen 	Research on d-limonene (DL) has moved from preclinical to Phase I and II clinical trials. DL is well tolerated by patients, and it accumulates in breast tissue at an average rate of 41.3 µg/g of tissue. A decrease in the expression of tumor cyclin D1 was established, which is associated with a stop in tumor proliferation. There is a dose-dependent increase in caspase-3 and annexin V only for ER-positive breast cancer cell lines (MCF-7).	(Chebet *et al.*, 2021; Lang *et al.*, 2011)
Oleanolic acid 	The mechanism of action of oleanolic acid (OA) and its derivatives is mainly directed against cancer cell proliferation, induction of apoptosis and autophagy, regulation of cell cycle regulatory proteins, inhibition of vascular endothelial growth, antiangiogenesis, and inhibition of tumor cell migration and invasion.	(Tang *et al.*, 2022)
Resveratrol 	Resveratrol (RV) protects DNA from reactive oxygen species (ROS), which trap hydroxyl and superoxide groups, as well as free radicals generated in cells. RV inhibits mitochondrial respiration in breast cancer cells. The cytotoxic effect of RV is modulated by SIRT1 and inhibition of mitochondrial complex I.	(Deus *et al.*, 2017; Leonard *et al.*, 2003)

The end of the table 2

Biologically active compounds	**Applications in Breast Cancer Therapy and mechanism of action**	**Experimental studies *in vitro*, *in vivo*. References**
Quercetin 	Quercetin (Qu) leads to apoptosis by mitochondrial cytochrome c. Suppresses the formation of cancer stem cells (RCCs), which are responsible for the recurrence of cancer. Qu inhibits metastasis by reversing EMT through MMP, TGFB1, and mTOR/c-Myc inhibition. Stabilization of the telomeric DNA structure and reduction of the P38MAPK and PI3K signaling pathways lead to the antiproliferative property of Qu.	(Ezzati *et al.*, 2020)
(−)-Epicatechin 	Treatment with (-)-epicatechin causes a decrease in MDA-MB-231 cell proliferation through an increase in reactive oxygen species (ROS), activation of the death receptors (DR4 and DR5), and an increase in pro-apoptotic proteins. In MCF-7 cell culture, a decrease in the viability of cancer cells occurs due to an increase in ROS and upregulation of proapoptotic proteins (Bad and Bax).	(Pereyra-Vergara *et al.*, 2020)
Cyanidin-3-O-glucoside 	Cyanidin-3-O-glucoside (C3G) inhibits EMT and the migration and invasion of breast cancer cells by upregulating Kruppel-like factor 4 (KLF4). KLF4 is involved in the regulation of proliferation, differentiation, apoptosis, and reprogramming of somatic cells. C3G attenuates breast cancer-induced angiogenesis by inhibiting VEGF.	(Chen *et al.*, 2020; Ma & Ning, 2019)
Delphinidin 	Delphinidin markedly inhibits the viability of HER-2 positive breast cancer cell lines by modulating cell cycle arrest and inducing apoptosis.	(Wu *et al.*, 2021)

Abbreviations: AKT – The collective name of a set of three serine/threonine-specific protein kinases; BAD – The BCL2 associated agonist of cell death protein; BAX – The Bcl-2-associated X protein; C-Myc – protein is a member of a family of proteins that regulate cell proliferation and apoptosis; DR4 and DR5 – Dead receptor 4 and Dead receptor 5; EMT – Epithelial-mesenchymal transition; MMP – Matrix metalloprotease; mTOR – Mammalian target of rapamycin signaling pathway; NF-κB – Nuclear factor kappa-light-chain-enhancer of activated B cells; P38MAPK – p38 mitogen-activated protein kinases; PI3K – Phosphoinositide 3-kinase; SIRT1 – Sirtuin 1; Sp1 – Specificity protein 1; TGFB – The transforming growth factor beta signaling pathway.

predominantly accumulates in breast tissue and induces apoptosis of ER-positive breast cancer cell lines (Lang *et al.*, 2011), but a systematic review of articles about the effect of D-limonene on breast cancer showed a lack of evidence base and requires additional placebo-controlled studies (Chebet *et al.*, 2021). Of the triterpenoids, oleanolic acid (Liang *et al.*, 2021), which is found in cranberries about 200 mg/100 g of fresh berries, has anti-tumor activity against BC. In his review article M. Ezzati *et al.* showed that quercetin can be used as natural compounds in the therapy of BC (Ezzati *et al.*, 2020). Flavonoids (Martinez-Perez *et al.*, 2014), anthocyanidins (Li *et al.*, 2022), phytosterols (Hutchinson *et al.*, 2019), procyanidins (Gao & Tollefsbol, 2018) have shown anti-cancer and chemo preventive effects against BC. There is a large number of researches on the effects of resveratrol against BC (Deus *et al.*, 2017; Gao & Tollefsbol, 2018). All these compounds are present to a greater or lesser extent in cranberry berries.

We found articles in the PubMed databases with the results of a study of the effects of lingonberry on cell proliferation in models of BC cell lines and epithelial cells of ectodermal origin (Olsson *et al.*, 2004; Rischer *et al.*, 2022; Wang *et al.*, 2005). Thus, lingonberry juice from Oregon (USA) in experiments with mouse skin epithelial cells significantly suppressed cancer transformation induced by 12-O-tetradecanoylphorbol-13-acetate (cancer promoter) and ultraviolet irradiation. This effect is attributed to the antioxidant properties of lingonberry juice and the anthocyanins and flavonoids it contains. Thus, lingonberry juice actively reduced peroxyl (ROO*), hydroperoxyl (*ON) radicals by 83.0% and reactive oxygen species by 99.0% from the cultured medium. It inhibits: AP-1 (activating protein-1) transcriptional activity via MARK (mitogen activating protein kinase) and NF-kB (universal transcription factor controlling expression of immune response, apoptosis and cell cycle genes). It should be noted that the average levels of phenolic compounds and anthocyanins in the juice of ripened lingonberry used in the experiment were 378.6 and 45.4 mg/100g, respectively. Based on the results of their studies, the authors conclude that lingonberry juice can be a very effective chemo preventive agent (Wang *et al.*, 2005). M.E. Olsson et al. found no effect of lingonberry extract from Sweden on the proliferative activity of estrogen receptor positive MCF-7 breast cancer cells (Olsson *et al.*, 2004). Finnish researcher H. Rischer et al. studied the chemical composition and effect of cell cultures of five northern berries: cloudberry, lingonberry, bearberry, arctic blackberry, strawberry on antioxidant activity and antiproliferative effects on MCF-7 breast cancer cells. Of the 5 cell cultures of these berries, lingonberries were significantly superior in anthocyanins, flavones and other flavonoids, phenolic acids, lignans, and total carotenoids. Lingonberry showed the highest antiproliferative activity against BC cells at concentrations of 200.0 and 300.0 μg/ml, reducing cancer cell growth by about 20.0%, and lingonberry at 600.0 μg/ml reduced cell growth by about 70.0%. Lingonberry has the highest antioxidant activity compared to the above 4 berries (Rischer *et al.*, 2022). Thus, lingonberry has an antiproliferative effect on BC cell cultures that is inferior in expression at lower concentrations to cloudberry, but significantly superior at higher concentrations. It should be noted that it is unlikely that the concentration of biologically active compounds of berries in human blood could reach the level that was used in the experiment to inhibit the development of cancer cells. Much more significant for practical health care is the effect of neutralization of carcinogens by lingonberry juice, due to the antioxidant activity of its nutrients. Benzoic acid isolated from Rubus fairholmianus berries was found to decrease viability and proliferative activity of MCF-7 breast cancer cells in vitro. Under the influence of this acid there was a release of cytochrome C, a change in mitochondrial membrane potential with subsequent induction of BC cell apoptosis (George, Abrahamse, 2019). In lingonberry, benzoic acid is found 73-158 mg/100g (Lyutikova & Botirov, 2015), which is a rather high level and is probably one of its chemical compounds with anticancer effects.

Conclusion

It should be noted that up to now, insufficient attention has been paid to the study of wild berries as prophylactic agents against BC. A methodologically flawless experimental study proved the role of lingonberries in inhibiting the development of carcinogen-induced epithelial cancer, and cell culture of lingonberry and cloudberry can reduce the viability and proliferative activity of BC cells. Lingonberry (*Vaccinium vitis-idaea L.*) and cloudberry (*Rubus chamaemorus*) are the most promising wild berries with protective potential to prevent this serious pathology. It cannot be ruled out that the traditionally constant level of their consumption by the native population of the region may be one of the reasons for the low incidence of BC. It is recommended to study the effect of extracts and juice of northern varieties of lingonberry and cloudberry on the development of BC cells as well as to identify chemical compounds with prophylactic and therapeutic effect.

Funding source: this work was supported by the Russian Science Foundation (grant No. 22-25-20032).

References

ANDERSEN Ø.M. (1985): Chromatographic Separation of Anthocyanins in Cowberry (Lingonberry) Vaccinium vites-idaea L. *Journal of Food Science* **50**(5), 1230–1232. doi: 10.1111/j.1365-2621.1985.tb10449.x.

BUJA A., PIERBON M., LAGO L., GROTTO G. & BALDO V. (2020): Breast cancer primary prevention and diet: An umbrella review. *International Journal of Environmental Research and Public Health* **17**(13), 1–54. doi: 10.3390/ijerph17134731.

BUJOR O.-C., GINIÈS CH. POPA V.I. & DUFOUR C. (2018): Phenolic compounds and antioxidant activity of lingonberry (Vaccinium vitis-idaea L.) leaf, stem and fruit at different harvest periods. *Food chemistry* **252**, 356–365. doi: 10.1016/j.foodchem.2018.01.052.

BYSTROVA E.A. & ALEKSEENKO E.V. (2017): Study of the component composition of phenolic compounds and antioxidant activity of lingonberry juice. *Izvestiya vuzov. Applied Chemistry and Biotechnology* **7**(3), 19–26. doi: 10.21285/2227-2925-2017-7-3-19-26. (In Russ.).

CAZAROLLI L., ZANATTA L., ALBERTON E., BONORINO FIGUEIREDO M.S., FOLADOR P., DAMAZIO R., PIZZOLATTI M. & BARRETO SILVA F.R. (2008): Flavonoids: prospective drug candidates. *Mini reviews in medicinal chemistry* **8**(13), 1429–1440. doi: 10.2174/138955708786369564.

CHANG V.C., COTTERCHIO M. & KHOO E. (2019): Iron intake, body iron status, and risk of breast cancer: a systematic review and meta-analysis. *BMC cancer* **19**(1), 543. doi: 10.1186/s12885-019-5642-0.

CHANGIZI Z., MOSLEHI A., ROHANI A.H. & EIDI A. (2021): Chlorogenic acid induces 4T1 breast cancer tumor's apoptosis via p53, Bax, Bcl-2, and caspase-3 signaling pathways in BALB/c mice. *Journal of Biochemical and Molecular Toxicology* **35**(2), 1–12. doi: 10.1002/jbt.22642.

CHEBET J.J., EHIRI J.E., MCCLELLAND D.J., TAREN D. & HAKIM I.A. (2021): Effect of d-limonene and its derivatives on breast cancer in human trials: a scoping review and narrative synthesis. *BMC cancer* **21**(1), 902. doi: 10.1186/s12885-021-08639-1.

CHEN D., YUAN M., YE Q., WANG X., XU J., SHI G. & HU Z. (2020): Cyanidin-3-O-glucoside inhibits epithelial-to-mesenchymal transition, and migration and invasion of breast cancer cells by upregulating KLF4. *Food & nutrition research* **64**. doi: 10.29219/fnr.v64.4240.

CHEN P., LI C., LI X., LI J., CHU R. & WANG H. (2014): Higher dietary folate intake reduces the breast cancer risk: a systematic review and meta-analysis. *British journal of cancer* **110**(9), 2327–2338. doi: 10.1038/bjc.2014.155.

CHESNOKOVA N.P., PONUKALINA E.V. & BIZENKOVA M.N. (2006): Sources of free radical formation and their significance in biological systems under normal conditions. *Modern High Technologies* **6**, 28–34. (In Russ.)

CORCORAN M.P., McKAY D.L. & BLUMBERG J.B. (2012): Flavonoid Basics: Chemistry, Sources, Mechanisms of Action, and Safety. *Journal of Nutrition in Gerontology and Geriatrics* **31**(3), 176–189. doi: 10.1080/21551197.2012.698219.

CUTRIM C.S. & CORTEZ M.A.S. (2018): A review on polyphenols: Classification, beneficial effects and their application in dairy products. *International Journal of Dairy Technology* **71**(3), 564–578. doi: 10.1111/1471-0307.12515.

DANDAMUDI A., TOMMIE J., NOMMSEN-RIVERS L. & COUCH S. (2018): Dietary patterns and breast cancer risk: A systematic review. *Anticancer Research* **38**(6), 3209–3222. doi: 10.21873/anticanres.12586.

DEUS C.M., SERAFIM T.L., MAGALHÃES-NOVAIS S. … & OLIVEIRA P.J. (2017): Sirtuin 1-dependent resveratrol cytotoxicity and pro-differentiation activity on breast cancer cells. *Archives of toxicology* **91**(3), 1261–1278. doi: 10.1007/s00204-016-1784-x.

DROZDZ P., ŠĖŽIENĖ V., WÓJCIK J. & PYRZYŃSKA K. (2017): Evaluation of Bioactive Compounds, Minerals and Antioxidant Activity of Lingonberry (Vaccinium vitis-idaea L.) Fruits. *Molecules* **23**(1). doi: 10.3390/molecules23010053.

DROZDZ P., ŠEZIENE V. & PYRZYNSKA K. (2017): Phytochemical Properties and Antioxidant Activities of Extracts from Wild Blueberries and Lingonberries. *Plant foods for human nutrition* **72**(4), 360–364. doi: 10.1007/s11130-017-0640-3.

EHALA S., VAHER M. & KALJURAND M. (2005): Characterization of phenolic profiles of Northern European berries by capillary electrophoresis and determination of their antioxidant activity. *Journal of agricultural and food chemistry* **53**(16), 6484–6490. doi: 10.1021/jf050397w.

ERMIS E., HERTEL C., SCHNEIDER C., CARLE R., STINTZING F. & SCHMIDT H. (2015): Characterization of in vitro antifungal activities of small and American cranberry (Vaccinium oxycoccos L. and V. macrocarpon Aiton) and lingonberry (Vaccinium vitis-idaea L.) concentrates in sugar reduced fruit spreads. *International Journal of Food Microbiology* **204**, 111–117. doi: 10.1016/j.ijfoodmicro.2015.03.017.

EZZATI M., YOUSEFI B., VELAEI K. & SAFA A. (2020): A review on anti-cancer properties of Quercetin in breast cancer. *Life Sciences* **248**, 117463. doi: https://doi.org/10.1016/j.lfs.2020.117463.

FARVID M.S., STERN M.C. … & CHO E. (2018): Consumption of red and processed meat and breast cancer incidence: A systematic review and meta-analysis of prospective studies. *International journal of cancer* **143**(11), 2787–2799. doi: 10.1002/ijc.31848.

GAO Y. & TPLLEDFSBOL T.O. (2018): Combinational Proanthocyanidins and Resveratrol Synergistically Inhibit Human Breast Cancer Cells and Impact Epigenetic−Mediating Machinery. *International journal of molecular sciences* **19**(8). doi: 10.3390/ijms19082204.

GEORGE B.P. & ABRAHAMSE H. (2019): Increased oxidative stress induced by Rubus bioactive compounds induce apoptotic cell death in human breast cancer cells. *Oxidative Medicine and Cellular Longevity. Hindawi* **2019**. doi: 10.1155/2019/6797921.

GRACE M.H., ESPOSITO D., DUNLAP K.L. & LILA M.A. (2014): Comparative analysis of phenolic content and profile, antioxidant capacity, and anti-inflammatory bioactivity in wild Alaskan and commercial Vaccinium berries. *Journal of agricultural and food chemistry* **62**(18), 4007–4017. doi: 10.1021/jf403810y.

GROSSO G., BELLA F., GODOS J., SCIACCA S., DEL RIO D., RAY S., GALVANO F. & GIOVANNUCCI E.L. (2017): Possible role of diet in cancer: systematic review and multiple meta-analyses of dietary patterns, lifestyle factors, and cancer risk. *Nutrition reviews* **75**(6), 405–419. doi: 10.1093/nutrit/nux012.

HEINONEN M. (2007): Antioxidant activity and antimicrobial effect of berry phenolics--a Finnish perspective. *Molecular nutrition & food research* **51**(6) 684–691. doi: 10.1002/mnfr.200700006.

HOSSAIN S., BEYDOUN M.A., BEYDOUN H.A., CHEN X., ZONDERMAN A.B. & WOOD R.J. (2019): Vitamin D and breast cancer: A systematic review and meta-analysis of observational studies. *Clinical nutrition ESPEN* **30**, 170–184. doi: 10.1016/j.clnesp.2018.12.085.

HUTCHINSON S.A., LIANTO P., MOORE J.B., HUGHES T.A. & THORNE J.L. (2019): Phytosterols Inhibit Side-Chain Oxysterol Mediated Activation of LXR in Breast Cancer Cells. *International journal of molecular sciences* **20**(13). doi: 10.3390/ijms20133241.

ISAAK C.K., PETKAU J.C., O K., DEBNATH S.C. & SIOW Y.L. (2015): Manitoba Lingonberry (Vaccinium vitis-idaea) Bioactivities in Ischemia-Reperfusion Injury. *Journal of agricultural and food chemistry* **63**(23), 5660–5669. doi: 10.1021/acs.jafc.5b00797.

ISAEV A.P. (2021): Prospects for the use of berry plants in Yakutia. In: *The role of botanical gardens in the conservation and enrichment of natural and cultural flora: Proceedings of the All-Russian Conference with international participation. Yakutsk, July 12–16, 2021*: North-Eastern Federal University named after M.K. Ammosova, 146–148. (In Russ.)

JIN B. (2022): Polyphenols and its Classification'. *Oxidants and Antioxidants in Medical Science* **11**(1), 1.

JOUYBARI L., KIANI F., AKBARI A., SANAGOO A., SAYEHMIRI F., AASETH J., CHARTRAND M.S., SAYEHMIRI K., CHIRUMBOLO S. & BJØRKLUND G. (2019): A meta-analysis of zinc levels in breast cancer. *Journal of trace elements in medicine and biology: organ of the Society for Minerals and Trace Elements (GMS)* **56**, 90–99. doi: 10.1016/j.jtemb.2019.06.017.

JUNGFER E., ZIMMERMANN B.F., RUTTKAT A. & GALENSA R. (2012): Comparing procyanidins in selected Vaccinium species by UHPLC-MS 2 with regard to authenticity and health effects. *Journal of Agricultural and Food Chemistry* **60**(38), 9688–9696. doi: 10.1021/jf303100q.

KARBYSHEV M.S. & ABDULLAEV K.P. (2018): *Biochemistry of oxidative stress: a teaching aid.* Moscow: XX, 60 pp. (In Russ.)
KELLY E., VYAS P. & WEBER J.T. (2018): Biochemical properties and neuroprotective effects of compounds in various species of berries. *Molecules* **23**(1). doi: 10.3390/molecules23010026.
KIM G.D. (2021): Ursolic Acid Decreases the Proliferation of MCF-7 Cell-Derived Breast Cancer Stem-Like Cells by Modulating the ERK and PI3K/AKT Signaling Pathways. *Preventive nutrition and food science* **26**(4), 434–444. doi: 10.3746/pnf.2021.26.4.434.
KIVIMAKI A.S., SILTARI A., EHLERS P.I., KORPELA R. & VAPAATALO H. (2014): Lingonberry juice negates the effects of a high salt diet on vascular function and low-grade inflammation. *Journal of Functional Foods* **7**(1), 238–245. doi: 10.1016/j.jff.2014.02.005.
KOROBKOVA T. S. (2017): Assessment of resource species of berry plants in the middle taiga subzone of Yakutia. *Eurasian Union of Scientists* **11**(44), 22–25. (In Russ.)
KOSTKA T., OSTBERG-POTTHOFF J.J., STÄRKE J. … & ESATBEYOGLU T. (2022): Bioactive Phenolic Compounds from Lingonberry (Vaccinium vitis-idaea L.): Extraction, Chemical Characterization, Fractionation and Cellular Antioxidant Activity. *Antioxidants* **11**(3). doi: 10.3390/antiox11030467.
KOWALSKA K. (2021): Lingonberry (Vaccinium vitis-idaea l.) fruit as a source of bioactive compounds with health-promoting effects—a review. *International Journal of Molecular Sciences* **22**(10). doi: 10.3390/ijms22105126.
KOWALSKA K., OLEJNIK A., ZIELIŃSKA-WASIELICA J. & OLKOWICZ M. (2019): Inhibitory effects of lingonberry (Vaccinium vitis-idaea L.) fruit extract on obesity-induced inflammation in 3T3-L1 adipocytes and RAW 264.7 macrophages. *Journal of Functional Foods* **54**(February), 371–380. doi: 10.1016/j.jff.2019.01.040.
KUMAR N. & GOEL N. (2019): Phenolic acids: Natural versatile molecules with promising therapeutic applications. *Biotechnology Reports* **24**, e00370. doi: https://doi.org/10.1016/j.btre.2019.e00370.
LANG J.E., MILLER J.A., NOKES B.T., LEBEAU L.G., DELBRIDGE M. & CHOW H.-H.S. (2011): P3-11-03: A Phase I Trial of D-Limonene in Newly Diagnosed Breast Cancer Patients: A Chemoprevention Study. *Cancer Research* **71**(24_Supplement), P3-11-03-P3-11–03. doi: 10.1158/0008-5472.SABCS11-P3-11-03.
LEE J. & FINN C.E. (2012): Lingonberry (Vaccinium vitis-idaea L.) grown in the Pacific Northwest of North America: Anthocyanin and free amino acid composition. *Journal of Functional Foods* **4**(1), 213–218. doi: https://doi.org/10.1016/j.jff.2011.10.007.
LEE K.-H., HO W.-Y., WU S.-J., CHENG T.-L., HUANG P.-J., WANG C.C.C. & HUNG J.-H. (2014): Behavior-selective Apoptotic Capacity of 4-(3,4,5-Trimethoxyphenoxy) Benzoic Acid and its Methyl Derivatives on Two Breast Cancer Cell Lines. *Anticancer Research* **34**(4), 1801-1809. Available at: http://ar.iiarjournals.org/content/34/4/1801.abstract.
LEONARD S.S., XIA C., JIANG B.-H., STINEFELT B., KLANDORF H., HARRIS G.K. & SHI X. (2003): Resveratrol scavenges reactive oxygen species and effects radical-induced cellular responses. *Biochemical and biophysical research communications* **309**(4), 1017–1026. doi: 10.1016/j.bbrc.2003.08.105.
LI W., PENG C., ZHAOJIE L. & WEI W. (2022): Chemopreventive and therapeutic properties of anthocyanins in breast cancer: A comprehensive review. *Nutrition research* **107**, 48–64. doi: 10.1016/j.nutres.2022.08.005.
LIANG Z., PAN R., MENG X., SU J., GUO Y., WIE G., ZHANG Z. & HE K. (2021): Transcriptome study of oleanolic acid in the inhibition of breast tumor growth based on high-throughput sequencing. *Aging* **13**(19), 22883–22897. doi: 10.18632/aging.203582.
LIU J., HEFNI M.E. & WITTHOFT C.M. (2020): Characterization of flavonoid compounds in common Swedish berry species. *Foods* **9**(3), 1–13. doi: 10.3390/foods9030358.
LIU Q., LUO L. & ZHENG L. (2018): Lignins: Biosynthesis and Biological Functions in Plants. *International journal of molecular sciences* **19**(2). doi: 10.3390/ijms19020335.
LUO J., HU Y.-L. & WANG H. (2017): Ursolic acid inhibits breast cancer growth by inhibiting proliferation, inducing autophagy and apoptosis, and suppressing inflammatory responses via the PI3K/AKT and NF-κB signaling pathways in vitro. *Experimental and therapeutic medicine* **14**(4), 3623–3631. doi: 10.3892/etm.2017.4965.

LYSENKO V. (2021): Oxidative stress as a non-specific factor in the pathogenesis of organ damage (Review of literature and own research). *Emergency Medicine* **16**(1), 24–35. doi: 10.22141/2224-0586.16.1.2020.196926. (In Russ.).

LYUTIKOVA M.N. & BOTIROV E.Kh. (2015): Chemical composition and practical application of lingonberries and cranberries. *Chemistry of plant raw material* **2**, 5–27. doi: 10.14258/jcprm.201502429. (In Russ.).

LYUTIKOVA M.N. (2013): *Study of the composition of biologically active components of wild berries Vaccinium Vitis-Idaea, Oxycoccus Palustris depending on their degree of maturity and storage conditions.* Author. diss. cand. chem. sciences, Surgut State University, 24 pp. (In Russ.).

MA X. & NING S. (2019): Cyanidin-3-glucoside attenuates the angiogenesis of breast cancer via inhibiting STAT3/VEGF pathway. *Phytotherapy research: PTR* **33**(1), 81–89. doi: 10.1002/ptr.6201.

MÄÄTTÄ-RIIHINEN K.R., KAMAL-ELDIN A., MATTILA P.H., GONZÁLEZ-PARAMÁS A.M. & TÖRRÖNEN A.R. (2004): Distribution and contents of phenolic compounds in eighteen scandinavian berry species. *Journal of Agricultural and Food Chemistry* **52**(14), 4477–4486. doi: 10.1021/jf049595y.

MALYSHEVA M.S. & SAMSONOVA I.V. (2022): Main trends in the development of the market for non-timber forest food resources in the Republic of Sakha (Yakutia). *Bulletin of the Altai Academy of Economics and Law* **3**, 224–234. doi: 10.17513/vaael.2120. (In Russ.).

MANE C., LOONIS M., JUHEL C., DUFOUR C. & MALIEN-AUBERT C. (2011): Food grade lingonberry extract: Polyphenolic composition and in vivo protective effect against oxidative stress. *Journal of Agricultural and Food Chemistry* **59**(7), 3330–3339. doi: 10.1021/jf103965b.

MARTINEZ-PEREZ C., WARD C., COOK G., MULLEN P., MCPHAIL D., HARRISON D.J. & LANGDON S.P. (2014): Novel flavonoids as anti-cancer agents: mechanisms of action and promise for their potential application in breast cancer. *Biochemical Society transactions* **42**(4), 1017–1023. doi: 10.1042/BST20140073.

MARTUSEVICH A.K. & KARUZIN K.A. (2015): Oxidative stress and its role in the formation of disadaptation and pathology. *Bioradicals and Antioxidants*, 5–18. (In Russ.).

MATTIO L.M., Catinella G., Pinto A. & Dallavalle S. (2020): Natural and nature-inspired stilbenoids as antiviral agents. *European Journal of Medicinal Chemistry* **202**, 112541. doi: https://doi.org/10.1016/j.ejmech.2020.112541.

NECHAEV A.A. (2018): Cowberry in the Far East: distribution, productivity, stocks of raw materials, development. In: *Perspectives of medicinal plant science: Proceedings of the International Scientific Conference dedicated to the 100th anniversary of the birth of Professor Alexei Ivanovich Schreter, Moscow, 01-02 November 2018*. Moscow: Federal State Budgetary Scientific Institution 'All-Russian Scientific Research Institute of Medicinal and Aromatic Plants', 121–129. (In Russ.).

NIKOLAEVA-GLOMB L., MUKOVA L., NIKOLOVA N., BADJAKOV I., DINCHEVA I., KONDAKOVA V., DOUMANOVA L. & GALABOV A.S. (2014): In vitro antiviral activity of a series of wild berry fruit extracts against representatives of Picorna-, Orthomyxo- and Paramyxoviridae. *Natural Product Communications* **9**(1), 51–54. doi: 10.1177/1934578x1400900116.

OLENNIKOV D.N., CHEMPOSOV V.V. & CHIRIKOVA N.K. (2022): Polymeric Compounds of Lingonberry Waste: Characterization of Antioxidant and Hypolipidemic Polysaccharides and Polyphenol-Polysaccharide Conjugates from Vaccinium vitis-idaea Press Cake. *Foods* **11**(18). doi: 10.3390/foods11182801.

OLSSON M.E., GUSTAVSSON K.-E., ANDERSSON S., NILSSON Å. & DUAN R.-D. (2004): Inhibition of cancer cell proliferation in vitro by fruit and berry extracts and correlations with antioxidant levels. *Journal of Agricultural and Food Chemistry* **52**(24), 7264–7271. doi: 10.1021/jf030479p.

PAL A., TAPADAR P. & PAL R. (2021): Exploring the Molecular Mechanism of Cinnamic Acid-Mediated Cytotoxicity in Triple Negative MDA-MB-231 Breast Cancer Cells. *Anti-cancer agents in medicinal chemistry* **21**(9), 1141–1150. doi: 10.2174/1871520620666200807222248.

PEREYRA-VERGARA F., OLIVARES-CORICHI I.M., PEREZ-RUIZ A.G., LUNA-ARIAS J.P. & GARCÍA-SÁNCHEZ J.R. (2020): Apoptosis Induced by (-)-Epicatechin in Human Breast Cancer Cells is Mediated by Reactive Oxygen Species. *Molecules* **25**(5). doi: 10.3390/molecules25051020.

PETROVA M.N. (2018): Peculiarities of seasonal nutrition in Yakutia. *International Journal of Applied and Basic Research* **10**, 84–90. (In Russ.).

POOROLAJAL J., HEIDARIMOGHIS F., KARAMI M., CHERAGHI Z., GOHARI-ENSAF F., SHAHBAZI F., ZAREIE B., AMERI P. & SAHRAEE F. (2021): Factors for the primary prevention of breast cancer: A meta-analysis of prospective cohort studies. *Journal of Research in Health Sciences* **21**(3). doi: 10.34172/jrhs.2021.57.

PRABBU S., MOLATH A., CHOKSI H., KUMAR S. & MEHRA R. (2021): Classifications of polyphenols and their potential application in human health and diseases. *International Journal of Physiology, Nutrition and Physical Education* **6**(1), 293–301. doi: 10.22271/journalofsport.2021.v6.i1e.2236.

QUIDEAU S., DEFFIEUX D., DOUAT-CASASSUS C. & POUYSÉGU L. (2011): Plant polyphenols: Chemical properties, biological activities, and synthesis. *Angewandte Chemie - International Edition* **50**(3), 586–621. doi: 10.1002/anie.201000044.

RASOULI H., FARZAEI M.H. & KHODARAHMI R. (2017): Polyphenols and their benefits: A review. International Journal of Food Properties. *Taylor & Francis* **20**(2), 1700–1741. doi: 10.1080/10942912.2017.1354017.

REN B., KWAH M.X.-Y., LIU C., … & GOH B.C. (2021): Resveratrol for cancer therapy: Challenges and future perspectives. *Cancer letters* **515**, 63–72. doi: 10.1016/j.canlet.2021.05.001.

REZAEI A., VARSHOSAZ J., FESHARAKI M., FARHANG A. & JAFARI S.M. (2019): Improving the solubility and in vitro cytotoxicity (anticancer activity) of ferulic acid by loading it into cyclodextrin nanosponges. *International journal of nanomedicine* **14**, 4589–4599. doi: 10.2147/IJN.S206350.

RISCHER H., NOHYNEK L., PUUPPONEN-PIMIÄ R., … & GRANATO D. (2022): Plant cell cultures of Nordic berry species: Phenolic and carotenoid profiling and biological assessments. *Food Chemistry* **366**, 130571. doi: https://doi.org/10.1016/j.foodchem.2021.130571.

RYYTI R., HÄMÄLÄINEN M., PELTOLA R. & MOILANEN E. (2020): Beneficial effects of lingonberry (Vaccinium vitis-idaea L.) supplementation on metabolic and inflammatory adverse effects induced by high-fat diet in a mouse model of obesity. *PLoS ONE* **15**(5), 1–17. doi: 10.1371/journal.pone.0232605.

SAVVIN A.A. (2005): *Food of the Yakuts before the development of agriculture (the experience of a historical and ethnographic monograph).* Yakutsk: IGI AS RS(Y), 376 pp. (In Russ.).

SEN A., ATMACA P., TERZIOGLU G. & ARSLAN S. (2013): Anticarcinogenic effect and carcinogenic potential of the dietary phenolic acid: o-coumaric acid. *Natural product communications* **8**(9), 1269–1274. doi: 10.1177/1934578x1300800922

SHEN N., WANG T., GAN Q., LIU S., WANG L. & JIN B. (2022): Plant flavonoids: Classification, distribution, biosynthesis, and antioxidant activity. *Food chemistry* **383**, 132531. doi: 10.1016/j.foodchem.2022.132531.

SZAKIEL A., PACZKOWSKI C. & HUTTUNEN S. (2012): Triterpenoid content of berries and leaves of bilberry Vaccinium myrtillus from Finland and Poland. *Journal of Agricultural and Food Chemistry* **60**(48), 11839–11849. doi: 10.1021/jf3046895.

TANG Z.-Y., Li Y., Tang Y.-T., Ma X.-D. & Tang Z.-Y. (2022): Anticancer activity of oleanolic acid and its derivatives: Recent advances in evidence, target profiling and mechanisms of action. *Biomedicine & Pharmacotherapy* **145**, 112397. doi: https://doi.org/10.1016/j.biopha.2021.112397.

TIKHONOV D.G., VINOKUROV M.M., KIPRYANOVA N.S. & GOLUBENKO M.V. (2022): The role of mitochondria in the development of breast cancer. *Russian Journal of Oncology* **27**(1), 207–221. (In Russ.).

TIKHONOV D.G., LEBEDEVA U. M. & STEPANOV K.M. (2019): From the history of the study of the diet in north-eastern Siberia: From the paleo diet to Coca-Cola in just 100 years. *History of Medicine* **6**(2), 63–69. doi: 10.17720/2409-5834.v6.2.2019.01a.

VERMERRIS W. & NICHOLSON R. (2009): Families of Phenolic Compounds and Means of Classification in Phenolic compound biochemistry. *Springer Science+Business Media B.V.* 1–34. doi: 10.5860/choice.45-0882.

VILCYCKYTE G., RAUDONE L. & PETRIKAITE V. (2020): Phenolic Fractions from Vaccinium vitis-idaea L. and Their Antioxidant and Anticancer Activities Assessment. *Antioxidants* **9**(12). doi: 10.3390/antiox9121261.

VILJANEN K., HEINIÖ R.-L., JUVONEN R., KÖSSÖ T. & PUUPPONEN-PIMIÄ R. (2014): Relation of sensory perception with chemical composition of bioprocessed lingonberry. *Food Chemistry* **157**, 148–156. doi: https://doi.org/10.1016/j.foodchem.2014.02.030.

VILKICKYTE G. & RAUDONE L. (2021): Vaccinium vitis-idaea l. Fruits: Chromatographic analysis of seasonal and geographical variation in bioactive compounds. *Foods* **10**(10), 1–22. doi: 10.3390/foods10102243.

VILKICKYTE G., PETRIKAITE V., PUKALSKAS A., SIPAILIENE A. & RAUDONE L. (2022): Exploring Vaccinium vitis-idaea L. as a potential source of therapeutic agents: antimicrobial, antioxidant, and anti-inflammatory activities of extracts and fractions. *Journal of ethnopharmacology* **292**, 115207. doi: 10.1016/j.jep.2022.115207.

VOLKOVA G.S., SERBA E.M., FURSOVA N.A., SOKOLOVA E.N., KUKSOVA E.V. & RIMAREVA L.V. (2018): Study of the qualitative composition of biologically active substances of cowberry fruits. *Voprosy pitaniya* **87**(5), 53–54. (In Russ.).

WANG S.Y., FENG R., BOWMAN L., PENHALLEGON R., DING M. & LU Y. (2005): Antioxidant activity in lingonberries (Vaccinium vitis-idaea L.) and its inhibitory effect on activator protein-1, nuclear factor-kappa B, and mitogen-activated protein kinases activation. *Journal of agricultural and food chemistry* **53**(8), 3156–3166. doi: 10.1021/jf048379m.

WANG S., CHANG X., ZHANG J., LI J., WANG N., YANG B., PAN B., ZHENG Y., WANG X., OU H. & WANG Z. (2021): Ursolic Acid Inhibits Breast Cancer Metastasis by Suppressing Glycolytic Metabolism via Activating SP1/Caveolin-1 Signaling. *Frontiers in oncology* **11**, 45584. doi: 10.3389/fonc.2021.745584.

WIBBERTMANN A., KIELHORN J., KOENNECKER G., MANGELSDORF I. & MELBER C. (2005): *Benzoic acid and Sodium Benzoate*. Concise International Chemical Assessment Document 26, Geneva.

WU A., ZHU Y., HAN B., PENG J., DENG X., CHEN W., DU J., OU Y., PENG X. & YU X. (2021): Delphinidin induces cell cycle arrest and apoptosis in HER-2 positive breast cancer cell lines by regulating the NF-κB and MAPK signaling pathways. *Oncology letters* **22**(6), 832. doi: 10.3892/ol.2021.13093.

XIAO Y., XIA J., LI L., … & SU X. (2019): Associations between dietary patterns and the risk of breast cancer: a systematic review and meta-analysis of observational studies. *Breast cancer research* **21**(1), 16. doi: 10.1186/s13058-019-1096-1.

ZENG A., LIANG X., ZHU S., LIU C., WANG S., ZHANG Q., ZHAO J. & SONG L. (2021): Chlorogenic acid induces apoptosis, inhibits metastasis and improves antitumor immunity in breast cancer via the NF-κB signaling pathway. *Oncol Rep* **45**(2), 717–727. doi: 10.3892/or.2020.7891.

ZHANG X., LIN D., JIANG R., LI H., WAN J. & LI H. (2016): Ferulic acid exerts antitumor activity and inhibits metastasis in breast cancer cells by regulating epithelial to mesenchymal transition. *Oncology reports* **36**(1), 271–278. doi: 10.3892/or.2016.4804.