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Study of various formulations, evaluation and pharmacological properties of Cowberry plant

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Abstract

Cowberry (*Vaccinium vitis-idaea* L., family Ericaceae) is a small evergreen shrub found in the herbaceous layer of circum boreal forests in Northern Eurasia and North America. It is sometimes cultivated, mainly in gardens, but more commonly its edible fruits are collected from the native habitats. Chemical composition in different aerial parts of *Vaccinium vitis-idaea* L., phenol glycosides, phenyl propanoids, anthocyanins, saponins have been found out by researchers from different countries; and in fruits, the content of anthocyanins has been established. Diuretics are the basic group of drugs for the treatment of patients with arterial hypertension, hypertensive crisis, etc. Diuretics have significant advantages in the form of a gradual increase in the diuretic effect and the lack of electrolyte loss. Diuretics, the cowberry are well received, which is widely used in folk medicine for the treatment and prevention of diseases of the urinary system. Anthocyanins are present in the outer layer of fruits, together with polyphenolic compounds, and a small content was found also in pulp and seeds.

Keywords: Cowberry plant, lingonberry, arbutin, phenolic acids, saponin phenylpropanoids

Introduction

Cowberry (*Vaccinium vitis-idaea* L., family Ericaceae) is a small evergreen shrub found in the herbaceous layer of circum boreal forests in Northern Eurasia and North America. *Vaccinium vitis-idaea*, the lingonberry, partridgeberry, mountain cranberry or cowberry, is a small evergreen shrub in the health. Lingonberry (*Vaccinium vitis-idaea* L.) is a low-bush wild plant found in the northern hemisphere. The berries contain vitamins (A, B1, B2, B3, and C), potassium, calcium, magnesium, and phosphorous and have a unique polyphenol composition, including flavonoids (Anthocyanins, flavonols {e.g., quercetin}, flavanols {catechins}), phenolic acids, lignans, stilbenes (Resveratrol), and phenolic polymers (e.g., proanthocyanidins) of which anthocyanins, flavonols, and proanthocyanidins are the main constituents. Resveratrol may be extracted from berry peels and seeds. Lingonberries contain particularly high amounts of anthocyanins: cyanidin-3-galactoside, cyanidin-3-arabinoside and cyanidin-3-glucoside. Polyphenols from berries are bioavailable from diet and they retain their biological activities in ileal samples. Lingonberry nutrient molecules show anti-cancerous, antimicrobial, antioxidative and anti-inflammatory effects [1]. Urinary tract infections are one of the most common infections that are widely found in outpatient and inpatient practice. Every year more than 150 million cases of urinary tract infections are registered in the world. According to a number of authors, the incidence of this pathology is 40% of all hospital infections. According to the World Health Organization (WHO), acute cystitis in women in Europe was in the second place in frequency after ARVI in official medicine, cowberry is used in the form of an infusion or decoction as a diuretic and disinfectant for inflammatory diseases of the bladder and the urinary tract. Cowberry drugs are recommended by the European Scientific Cooperative on phytotherapy (ESCOP) and the German Commission Monographs for the treatment of dysuria disorders and cystitis in cases where there are no indications for the use of antibiotics [2]. Flavonoids such as Anthocyanins, flavones glycosides, and proanthocyanidins are currently considered to be the health-promoting constituents of the berries. Among ericaceous berry fruits, lingonberries Exhibit intermediate levels of anthocyanins and flavones glycosides but high content of procyanidins compared to bilberries (*Vaccinium vitis* L.). Lingonberry extracts have been found to inhibit the promotional stage of chemically induced carcinogenesis, the intestinal tumor genesis in multiple intestinal neoplasia, the growth of periodontal pathogens, the hemagglutination of Escherichia coli, the aggregation of oral bacterial cells, and the binding of neisseria meningitidis pili to human epithelial cells [3]. Cowberry is evergreen the leaves are tough, smooth and have a thick cuticle.

Cowberry grows on both, dry, humus-poor soils, on raw humus and even on peat soils. Cowberry has needle-like, narrow, evergreen leaves. It grows at approximately the same sites as cowberry from nutrient-poor, light dry heaths to ombrogenous peat and peaty podzols. Cowberry is known to be very heavy metal resistant. It can influence the establishment of other species. Its leaf extracts are allelopathic to prohibit, for example, the establishment of Scots pine seedlings^[4]. The *Genus vaccinium* L., which comprises approximately 450 species worldwide includes three recently domesticated crops lingonberries (*V. vitis-idaea* L.), blueberries and cranberries. Lingonberries are widely distributed dwarf woody shrubs found mainly in Europe and Asia, with a few species inhabiting arctic-montane regions. Lingonberry, also known as cowberry, foxberry, rock cranberry, redberry and partridgeberry, is thought to be a circumboreal cranberry blueberry intermediate. From time immemorial, humans have gathered wild lingonberry fruits. These fruits have served as a source of juice, iced wine, jelly and jam, and have also been preserved and used as a condiment with meat. Both lingonberry fruits and leaves are full of phenolic compounds, such as flavonoids and aromatic acids. Because of their nutritional properties, lingonberries

have been considered potential materials for nutraceuticals and have been used to treat inflammatory diseases and wounds. Lingonberries grow naturally under a wide range of ecological conditions, thus allowing *Vaccinium* crops to be cultivated further north than previously possible^[5]. Anthocyanins are responsible for almost all the red, blue and purple colors exhibited by flowers, fruits and other plant tissues. As a result of the continuing official delisting of artificial food dyes, there has been increased interest in the use of these water-soluble plant pigments as food colorants^[6]. The promising plant to create a new herbal medicine is cowberry (*Vaccinium vitis-idaea* L.), its resources are sufficient in Ukraine. In traditional and official medicine a decoction of cowberry leaves is used as a highly effective medicine for the treatment of diseases of the kidney and the urinary tract. It is commonly known that phenolic compounds are the main group of substances with the pharmacological action of this medicinal plant raw material. The qualitative and quantitative chemical determination of some classes in leaves and extracts of cowberry. They are simple phenols, derivatives of hydroxycinnamic acid, flavonoids, polyphenolic compounds and organic acids^[7].



Fig 1: Cowberry plant^[31].

Plant Description

Chemical composition in different aerial parts of *Vaccinium vitis-idaea* L., phenol glycosides, phenylpropanoids, anthocyanes, and saponins have been found out by researchers from different countries; and in fruits, the content of anthocyanes has been established.

Phytochemicals of Vaccinium Fruits

Anthocyanin

Anthocyanins are present in the outer layer of fruits, together with polyphenolic compounds, and a small content was found also in pulp and seeds. Environmental factors can affect the content and composition of secondary metabolites in berries. Growing conditions also affect the content of anthocyanins and other phenolic compounds in the berries of wild and cultivated species. Before berry ripening, proanthocyanidins, flavonols and hydroxycinnamic acids are the major phenolic compounds. During the ripening process, flavonoid profiles vary, and anthocyanins accumulate in the skin. High levels and a wide variety of anthocyanins provide the red, blue, and purple colors that characterize berries of this genus. *Vaccinium* berries have a well-deserved reputation as potential healthy products and functional foods, supported by many studies, which have identified and quantified various bioactive phytochemicals with known benefits for human health. Many studies have demonstrated the benefits of anthocyanin-rich extracts of *vaccinium* species in the prevention of several diseases [8]. Anthocyanins are commonly found in plant tissues, producing blue, red and purple colours. They are the most important water-soluble pigments in plants. Among edible plants, berries (grape, cherry and plum included) with red, blue or purple colours constitute one of the most important sources of anthocyanins.

In an earlier study, we showed that anthocyanins are especially abundant in cowberry. Several other berries also have high contents, among them blackcurrant, cowberry, chokeberry, cranberry and cowberry [9].

Flavonoids

Flavonoids are formed in plants from the aromatic amino acids phenylalanine and tyrosine, and malonate. The basic flavonoid structure is the flavonoid nucleus, which consists of 15 carbon atoms arranged in three rings (C₆ C₃ C₆). The various classes of flavonoids differ in the level of oxidation and pattern of Substitution of the C ring, while individual compounds within a class differ in the pattern of substitution of the A and B rings. Flavonoids are among the most ubiquitous Phenolic compounds found in the *genus vaccinium*. The structures vary based on the substituent of hydroxyl at the B ring, as well as the nature and the number of sugars attached to the molecule. To date, more than 50 compounds have been isolated and identified from the *genus vaccinium*. Flavonoid glycosides are one of the most frequently Chemical constituents from *Vaccinium* [10]. Flavonoids are a wide range of phytochemicals with various pharmacological effects including antioxidant, anti-inflammation, anti-platelet, anti-allergic, cytotoxicity, reduce risk for heart disease or cancer etc. These flavonoids inhibited various enzymes such as prostaglandin synthase, lipoxygenase, and cyclooxygenase, and induced detoxifying enzyme systems such as glutathione S-transferase. Flavonoids have significant vitamin C-sparing activity and more powerful antioxidants than traditional vitamins such as quercetin, myricetin, rutin and apigenin. In vegetables, quercetin glycosides predominate, but glycosides of kaempferol, luteolin, and apigenin are also present [11].

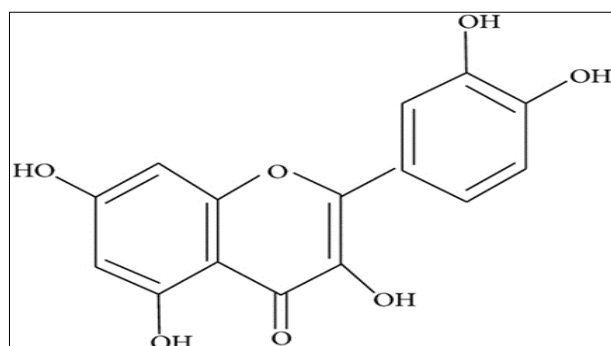


Fig 2: Structure of Flavonoids

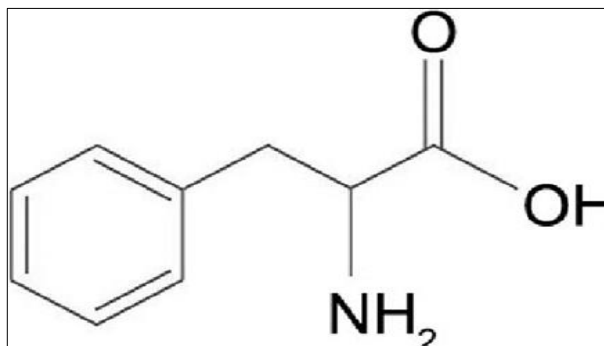


Fig 3: Structure of Phenylalanine.

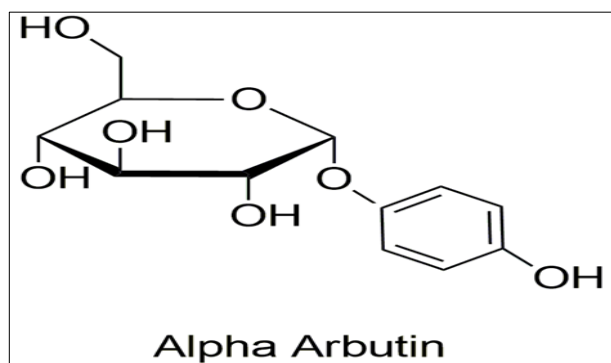


Fig 4: Structure of Alpha Arbutin

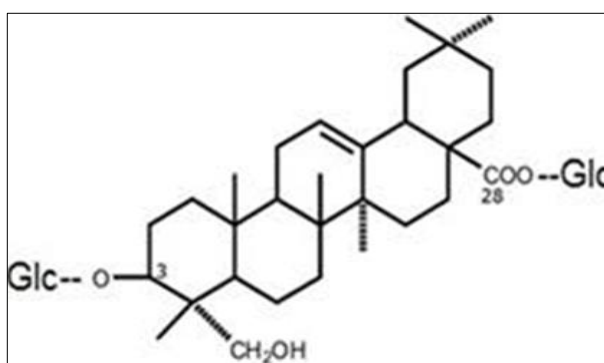


Fig 5: Structure of Saponin

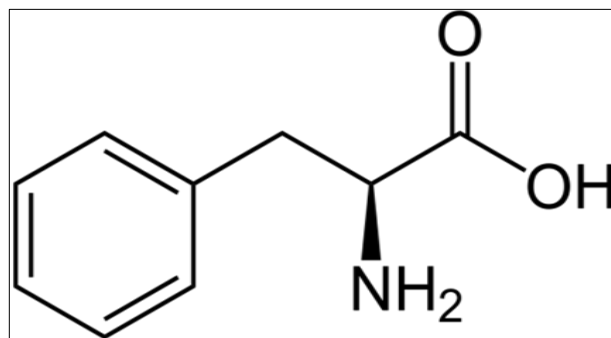


Fig 6: Structure of phenylpropanoids

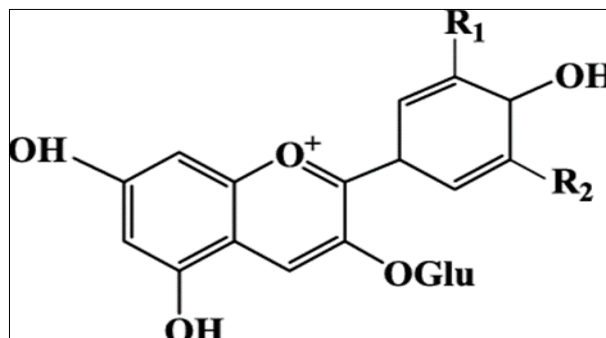


Fig 7: Structure of Anthocyanins

In the leaves of cowberry

Arbutin

In the leaves of cowberry arbutin, methyl arbutin, Flavonoids and ursolic acid are present, whilst in fruits there are organic acids, tannins, carbohydrates and vitamins A and C. Products prepared from cowberry disinfect the urinary bladder and tracks, Act diuretically and statistically. The aim of this study was the use of densitometry for the quantitative determination of arbutin in the Leaves of cowberry (*Vaccinium vitis ideas*). Arbutin is a hydroquinone derivative with Molecular formula C₁₂H₁₆O₇. It shows significant Therapeutic activity. Arbutin is, among others, an antibacterial agent of the urinary tract. It is also used in Cosmetic preparations as a component causing Whitening in melanosis^[12].

Method of Preparation

Classification

Sr. No	Classification	Scientific name and Common name
1.	Kingdom	Plantae/ Plant
2.	Subkingdom	Tracheobionta- Vascular plants
3.	Super division	Spermatophyta-Seed plants
4.	Division	Magnoliophyta-Flowering plants
5.	Class	Magnoliopsida-Dicotyledons
6.	Subclass	Dilleniidae
7.	Order	Ericales
8.	Family	Ericaceae juss- Health Family
9.	Genes	<i>Vaccinium L.</i> - blueberries, Huckleberry.
10.	Species	<i>Vaccinium vitis-idaea L.</i> lingonberry.

Cowberry Nutrition

Raw lingonberries are 86% water, 13% carbohydrates 1% protein and contain negligible fat. In 100 grams lingonberries supply 228 calories and are low-to-moderate sources of vitamin C, B vitamins, and dietary minerals.

Lingonberries contain the following nutrients per 100 grams (g)

Nutrients	Amount
Calories	56
Protein	0.5 g
Fat	0.7 g
Carbohydrates	8.9 g
Fibre	2.6 g
Vitamin C	10.7 g
Vitamin E	1.5 g

Cultivation and collection of cowberry

There are some cultivars produced, but there is no large-scale cultivation, and plant breeding of lingonberry is still in its infancy. Cultivation of lingonberry can best meet the increased needs of plant material. To optimize horticulturally

important traits, evaluation of the phytochemical differences between cultivated and wild lingonberries is needed, as well as emphasis on factors such as optimal collecting time and environmental conditions leading to better yield. The obtained results will be really important to breeders for developing new cultivars and, of course, as a part of the ongoing interest in nutritional and nutraceutical properties of food, the content of sugars in lingonberries will be of interest to dietitians and may be used in the pharmaceutical industry in developing new products for consumers with special dietary requirements^[13]. Lingonberries were first cultivated in 1789 but intensive efforts have been initiated only recently to develop a high-quality horticultural fruit crop. In the past, all fruit was collected from wild stands. Domestication of the lingonberry is potentially valuable in providing large quantities of high-quality berries for commercial processing. Cultivation practices can reduce labour costs and provide a reliable supply of berries for domestic and export markets for fresh and processed fruit. For the home gardener, domestication of the lingonberry can lead to the development of an attractive home landscape plant that will produce an accessible crop of fruit for fall harvesting. However, considerable research is required, both for the development of a small-fruit industry and for home gardening use, if the lingonberry is to be effectively adapted from a wild plant into a cultivated, high-quality, horticultural crop^[14].

Material and Methods

Plant and soil material

Plant material and soil samples were randomly collected from the natural habitat in the white forest. Fresh whole plants were manually divided into organs: leaves stems and rhizomes. Berries were harvested separately as ripe fruits. All collected material was dried at 40 °C and weighed. Plant parts were powdered in a laboratory mill.

Extraction

Cowberry fruits, leaves, stems and rhizomes as well as soil samples were extracted in a Soxhlet apparatus for 6 hours at first with ethyl ether, and afterwards with methanol. Ether extracts were evaporated to dryness immediately, whereas to the obtained methanol extracts equal volumes of water were added, methanol was evaporated and the remaining aqueous solutions were extracted four times with n-butanol.

Separation

The obtained mixtures were fractionated on a column (CC) using silica gel, 30–70 mesh in an increasing-polarity step gradient of hexane/ethyl ether (for the ether extracts) or chloroform/methanol (for butanol extracts) and afterwards rechromatographed by TLC (silica gel; chloroform/methanol, 98: 2, v/v; chloroform/ methanol, 85: 15, v/v;

chloroform/methanol/water 61: 32: 7, by vol.). Compounds were localized on plates by comparison to standards. Free triterpene acids were eluted from the gel with ethyl ether. Fractions of derivatives were eluted with methanol and subjected to hydrolysis [15].

Fruit Samples and Their Extractions

Fruit samples and their extraction fruits of wild-growing lingonberries were collected at commercial ripeness from pine forests during September of 2016, in three different locations in the Mazovia region. The limited area central part of the local marketplace. Fruits after homogenization by blender were stored at $-20\text{ }^{\circ}\text{C}$ until bioactive substances were analyzed. Then, the extracts were filtered through whatman no. 1 Filter paper. For a given sample, three independent extractions using an appropriate solvent were carried out.

Total phenolic Content

Total phenolic content of extracts was assessed by using the Folin Ciocalteu (FC) reagent method. Then, 0.1 ml of extract was mixed with 0.1 ml of FC reagent and 0.9 ml of water. After 5 min, 1 ml of 7% (w/v) Na_2CO_3 and 0.4 ml of water were added. The extracts were mixed and allowed to stand for 30 min before measuring. The absorbance was measured after 30 min at 765 nm using the lambda Bio 20 spectrophotometer. A mixture of water and reagents was used as a blank. Total phenol content was expressed as gallic acid equivalents in mg/100 g of fresh fruits.



Fig 8: Jam of cowberry plant

Evaluation

Bilberry and cowberry yields were assessed, in a pairwise manner, on the basis of slides showing the stands of this study ($n = 100$). Pair-wise comparisons were carried out and analyzed using an application of the method developed by Alho *et al.* (2000). Before composing the pairs, the slides were randomized and marked with the labels 1; 2; n. The pairs were formed so that the slide number 1 was compared to the slide number 2, 2 to 3, n 1 to n. Then the comparisons 1 to 3, 2 to 4, and n 2 to n were added. Thus, the total number of pairs was $(n - 1) \times n / 2 = 197$. Finally, the order in which the pairs

were presented to the evaluators was randomized. The slides were evaluated at meetings organized for three groups of persons: forest professionals (7 persons), berry pickers (10) and members of a nature-society (10). These people were expected to be experts in assessing the berry yields of different forest stands. Each pair of slides to be examined and compared with each other was projected onto the same screen, the slides adjacent to each other, for a period of 15–17 s, which was found to be sufficient for assessing both bilberry and cowberry yields. First, the evaluators assessed which of the two forest stands displayed produces a better bilberry yield and how much better the yield in one stand is compared to that of the other stand. Then they conducted the corresponding assessment with respect to the cowberry yield. The following verbal scale was used: (i) equal priority of both stands, (ii) weak priority of one stand over another, (iii) strong priority of one stand over another, (iv) demonstrated priority of one stand over another, and (v) absolute priority of one stand over another. Verbally expressed priorities were translated into numerical values of 1:1, 3:1, 5:1, 7:1, and 9:1, respectively (equal priority is 1:1, weak priority is 3:1, absolute priority is 9:1). The numerical ratios of 2:1, 4:1, 6:1, and 8:1 were used as intermediate values [33].



Total Flavonoids Content

Total flavonoids content was determined using a spectrophotometric method based on the formation of flavonoids complex with Al^{3+} ions. First, 1 ml of a sample was mixed with 0.3 ml of NaNO_2 (5%, w/v) and 0.5 ml of AlCl_3 (2%, w/v). A sample was mixed and six minutes later was neutralized with 0.5 ml of 1 mol/L NaOH solution. The mixture was left for 10 min at room temperature and then absorbance was measured at 510 nm. The results were expressed as catechin equivalent (CE) in μmol Per 100 g of fruit.

Total Monomeric Anthocyanins

The total monomeric anthocyanins content was determined using the pH-differential method. The change of absorbance at 518 nm was recorded after 30 min. The DPPH scavenging percentage was calculated according to expression $(A_0 - A_s)/A_0 \times 100$, where A_0 is the initial absorbance of the DPPH methanolic solution and A_s is the absorbance of the test sample. The cupric ion-reducing antioxidant capacity of all extracts was determined according to the method of Apak *et al.* The mixture was incubated in a water bath at the temperature of $50\text{ }^{\circ}\text{C}$ for 20 min. The calibration curve was made with trolox and the antioxidant activity was expressed as mm of trolox per gram of fresh fruits. Statistical Analysis to verify the statistical significance, the mean \pm SD of three independent measurements was calculated. Differences between groups were tested two-way [16].

Leaves samples and their Extraction Samples, Standards, and Chemicals

Lingonberry and (*Vaccinium vitis-idaea*) extracts were obtained from as finished products derived from successive steps of extraction, purification, concentration, and spraydrying. Standard molecules of (p)-catechin and (-)-epicatechin as well as reagent were supplied by rutin and quercetin as well as acetic acid, hydrochloric acid, and anhydrous sodium carbonate, cyanidin-3-O-galactoside (idea in chloride), cyanidin-3-O-glucoside (kuromanin), peonidin-3-O-glucoside, procyanidin B1, procyanidin B2, and procyanidin A2. Peonidin-3-O-galactoside and cyanidin-3-O-arabinoside). HPLC-grade acetonitrile, as well as methanol, formic acid, and orthophosphoric acid [32].

Leaves of cowberry plant

Tea is an excellent natural source of antioxidants, and phenolic compounds represent the most abundant group. Indeed, tea is particularly rich in terms of flavonoids, such as flavanol monomers (catechin, epicatechin) and flavanol gallates (epicatechin gallate, epigallocatechin gallate). Apart from the mentioned analytes, tea contains as well other polyphenols to a lesser amount, such as gallic acid, coumaric acid and caffeic acid, as well as purine alkaloids, theobromine and caffeine. There are different types of tea according to the manufacturer green, black, white and oolong teas. There are different methods for carrying out its production, and thus, a wide variety of products based on the catechins oxidation degree. Liquid chromatography with UV absorbance or MS detection has been the method selected more often for analysing phenolic compounds in tea. [pdf no 26].

Arbutin

Plant material leaves of cowberry were collected in 2005 and 2006 year. They were dried to constant mass in the form of thin layers permeable to air and shaded place. Preparation of extract of cowberry leaves To 1 g of powdered material 5 ml of water methanol solution (1:1, v/v) was added and then the solution was refluxed for 15 min. The hot solution was filtered and washed with 5 ml of methanol. Then it was cooled down and 0.5 g of lead (IV) hydroxyl acetate was added. The final volume of extract was 10 ml. Preparation of standard solution of arbutin Standard solution of arbutin was prepared by dissolving 60 mg of arbutin in 10 ml of methanol. Quantitative determination of arbutin in the extract of cowberry leaves the internal standard solution method was used. The following solutions were prepared [17].

Pharmacological Properties of Cowberry Plant

Antioxidant activity

Lingonberry seed oil improves the skin's hydration making skin smoother and younger looking making skin smoother and younger looking. Omega 3 and 6 acids in lingonberries help to reduce water loss significantly and many actives in the lingonberry seed oil act as antioxidants, blocking free radicals that can damage skin. A significant number of experimental researches have been devoted to the investigation of the antioxidant properties Of *Vaccinium vitis-idaea* extracts. So, the tannins obtained from *Vaccinium vitis-idaea*, can inhibit the processes of lipid peroxidation, which was confirmed by a decrease in the formation of thiobarbituric acid-active products. In This study, the inhibitory properties of *Vaccinium vitis-idaea* tannins against superoxide radical (xanthine oxidase inhibition test) have also been established [18]. Lingonberries had a high content of antioxidants, and

cyanidin 3-galactoside was the most dominant anthocyanin, contributing the most antioxidant activity in lingonberries. Anthocyanins and phenolics are secondary plant metabolites. They protect the plant against damaging photodynamic reactions by quenching the excited state of active oxygen species. Anthocyanins are probably the largest group of phenolic compounds in the human diet and have been used for several therapeutic purposes including the treatment of diabetic retinopathy, fibrocystic disease, and vision disorders. Anthocyanins also have the potential to serve as radiation protective agents, vasotonic agents, and chemo protective agents and decrease the fragility of capillaries inhibit blood platelet aggregation, and strengthen the collagen matrix of connective tissues [19].

Antimicrobial activity

Antimicrobial activity was assayed by the agar dilution method using BHI agar (Difco Laboratories) supplemented with 0.5% yeast extract, 10 mg mL⁻¹ vitamin K, 5 mg mL⁻¹ hemin and 5% sheep red blood cells. Before testing, bacteria were inoculated with Llin in the same medium and incubated for 3–4 days at 35 °C. The highest concentration of tannin or tetracycline in serially-diluted solution was 100 µg mL⁻¹. Media containing tannin was prepared by adding 1 vol. of two-fold serially-diluted tannin solution (in 50% dimethylsulfoxide) to 9 vols. BHI agar that had been warmed to 50 °C and supplemented with vitamin K hemin and sheep red blood cells as described above. Agar plates containing tannin, a control plate without tannin and a positive control plate containing tetracycline were spot inoculated with 10⁴ CFU mL⁻¹ with a steers replicator immediately after preparation of the inocula [20]. The antimicrobial effects of cowberry concentrates are well known and have been described to act against bacterial pathogens such as *E. coli* O157:H7, and *L. monocytogenes*, and *Staphylococcus aureus*. Berries contain a number of bioactive compounds such as vitamins, minerals, anthocyanins, flavonols, phenolic acids, catechins, ellagic and Gallic acid, quercetin, tannins, and others. In this study, we determined the amount of sodium benzoate in concentrates made of both berries. Although the sodium benzoate content may be responsible for the antifungal effects, other compounds may be involved. Only a few studies with lingonberry extract to inhibit fungal growth in foods [21].

Antibacterial activity

Among cultivated lingonberry (*Vaccinium vitis-idea*) is known to prevent the adhesion of *Escherichia coli*, *Helicobacter pylori*, and mutant streptococci. The anti-adhesion activity of cranberry has been attributed to carbohydrates as well as to high molecular weight material and to polyphenols such as proanthocyanidins. Among other fruits orange and pineapple juice, guava lectins, and blueberry proanthocyanidins are known to have effects against the binding of *E. coli in vitro* and the polysaccharides from black currant seeds against *H. pylori in situ*. Berries are known as rich sources of polyphenols, such as anthocyanin, proanthocyanidins, and flavonols. Because of increasing antibiotic resistance and the lack of effective vaccines, new prevention methods against bacterial diseases are needed. The strategy of preventing the first step of infection, by blocking the adhesion of pathogens to host surfaces, provides novel potential to control infectious diseases. The aim of the present study was to investigate several berries and fruits as potential sources of anti-adhesives against *N. Meningitis* together with

chemical characterization of the berry and fruit samples [22]. *Vaccinium vitis-idaea* (lingonberry) leaves extracts against uropathogenic *E. coli* rods as well as their impact exerted on virulence factors and bio film formation. *Vaccinium vitis-idaea* extracts on bacterial survival and virulence factors involved in tissue colonization and bio film formation of the neuropathogenic *Escherichia coli* rods [23].

Anti-inflammatory

Arbutin (ARB), a natural antioxidant extracted from the Chinese medicine herb cowberry leaf, can suppress inflammation via inhibiting the NF- κ B pathway in animal models of diabetes, demyelination, and acute lung injury. Moreover, ARB can protect cells against oxidation via activating Nrf2. Although ARB has been studied in many disorders, the anti-inflammation feature of ARB on chondrocytes and its effects on treating OA have not been explored. Yet, ARB is prone to oxidization and decomposition under acidic conditions, as that in an OA joint. To overcome these drawbacks, a novel vectors needed to protect ARB from oxidization and achieve sustained release [24]. Lingonberries (*Vaccinium vitis-idaea* L.) in the diet, like other berries, are thought to have beneficial health effects. They contain phenolic substances and several *in vitro* and *in vivo* studies show e.g. Antioxidative, antimicrobial, anti-inflammatory, anticancerous and improved hepatic function and glycemia [effects of lingonberries, but to our knowledge scarce clinical studies have been conducted on the effects to the oral cavity. Examples of an elevated inflammatory or infection Risk include patients suffering from general conditions such as diabetes. Neutrophil collagenase/collagenase-2 or matrix metalloproteinase (MMP)-8 is a collagenolytic and immunomodulatory proteolytic enzyme, and elevated levels of its active form reflect [25].

Neuroprotective activity

The plant species belong to the family Ericaceae and *genus vaccinium* and are known to have numerous health benefits. The present work aims to study the polyphenolic content, antioxidant capacity, and potential neuroprotective effects of fruit and leaf extracts from lingonberries (also known as partridgeberries). Initial chemical analysis, cell cultures derived from rodent brains were subjected to high levels of glutamate, the most prominent endogenous excitatory neurotransmitter present in the mammalian central nervous system. Glutamate-induced "excitotoxicity" is a pathological process by which cells are damaged and killed by excessive stimulation from neurotransmitters such as glutamate and similar substances. This abnormal process produces oxidative and nitrosative stress and likely contributes to the pathology of traumatic brain injury, stroke, and neuro degenerative disorders [26].

Antidiabetic activity

Natural products from fruit and vegetable sources are becoming popular worldwide and broadly accepted as an aid to conventional therapy. Increasing public awareness and scientific interest headed the research towards the evaluation of fruits' role in health upgradation and disease treatment. In recent years, great attention has been focused on the health-promoting roles of bioactive components known as "flavonoids". Flavonoids are ubiquitously secondary metabolites present in almost all fruits and vegetables antidiabetic mechanism of flavonoids might be mainly due to

their effects on enzymes responsible for glucose metabolism or through other novel mechanisms still to be explored. Importantly, flavonoids exert antidiabetic action by ameliorating the insulin action on skeletal muscle and liver cells to reduce the plasma-free fatty acid level, hepatic gluconeogenesis, and increased glucose uptake. In the intestine, flavonoids inhibit the digestion of starch, slow down gastric emptying, and reduce the absorption of glucose across the membrane. The regulation of postprandial hyperglycemia is an important strategy for diabetes management. Such an approach is to reduce the digestion (intestinal) of complex carbohydrates (disaccharides oligosaccharides, and trisaccharides) by inhibiting the activity of intestinal membrane-bound α -glucosidases [27].

Antineoplastic activity

The most promising anticarcinogenic agents in plants are phenolic compounds, which are abundant in berries. Concomitantly, berries and their extracts have been shown to be chemopreventive at several stages of the carcinogenic process. In the Nordic countries, wild berries are easily available and commonly consumed. In Finland, the incidence of colorectal cancer differs up to 2-fold between the North and the South, Which is accompanied by higher consumption of wild berries in the North. To study the possible chemopreventive properties of Wild berries and their effects on spontaneous intestinal tumor formation in the Min/1 mouse, we studied 3 berries with different phenolic profiles: bilberry [(BB), 7 *Vaccinium*], lingonberry (LB, *Vaccinium vitis-idaea*), and cloudberry (CB, *Rubus chamaemorus*), which are rich in anthocyanins, Proanthocyanidins, and ellagic acid, respectively [28].

Cowberry in Cancer

Uncontrolled proliferation and suppressed apoptosis are important steps in the initiation and progression of cancers. The antiproliferative effectiveness of a range of fruit extracts enriched in polyphenols, but devoid of vitamin C and carotenoids, using a screen based on the growth of human cervical carcinoma (He La) cells with comparative studies on human colon cancer (CaCo-2) cells [29]. Lingonberry (*Vaccinium vitis-idaea*) and bilberry (*Vaccinium myrtillus*) are common dietary fruits and their biochemical composition, with the proportion of anthocyanins being considerably high in bilberry and that of proanthocyanidins. In lingonberries of the richest dietary sources of polyphenols, especially anthocyanins, in Finnish diets. The objective of this systematic review was to collect current English-written scientific research on the anticancer effects of lingonberry and bilberry on digestive tract cancers [30].

Discussion and Conclusions

Prediction models for cowberry yields a separate model was created for cowberry yields. Indicated that forests of *vaccinium* type or poorer produced the best cowberry yields. Volume had a positive effect on cowberry yields. The basal area of deciduous trees had a negative effect on cowberry yields. They are collected from the wild, and plant breeding of lingonberry was still on a small scale. However, lingonberry had the highest antioxidants content among berries and possesses a broad range of health-promoted effects. The introduction of lingonberries to the daily diet could have a positive health effect, especially for patients suffered from civilization diseases.

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