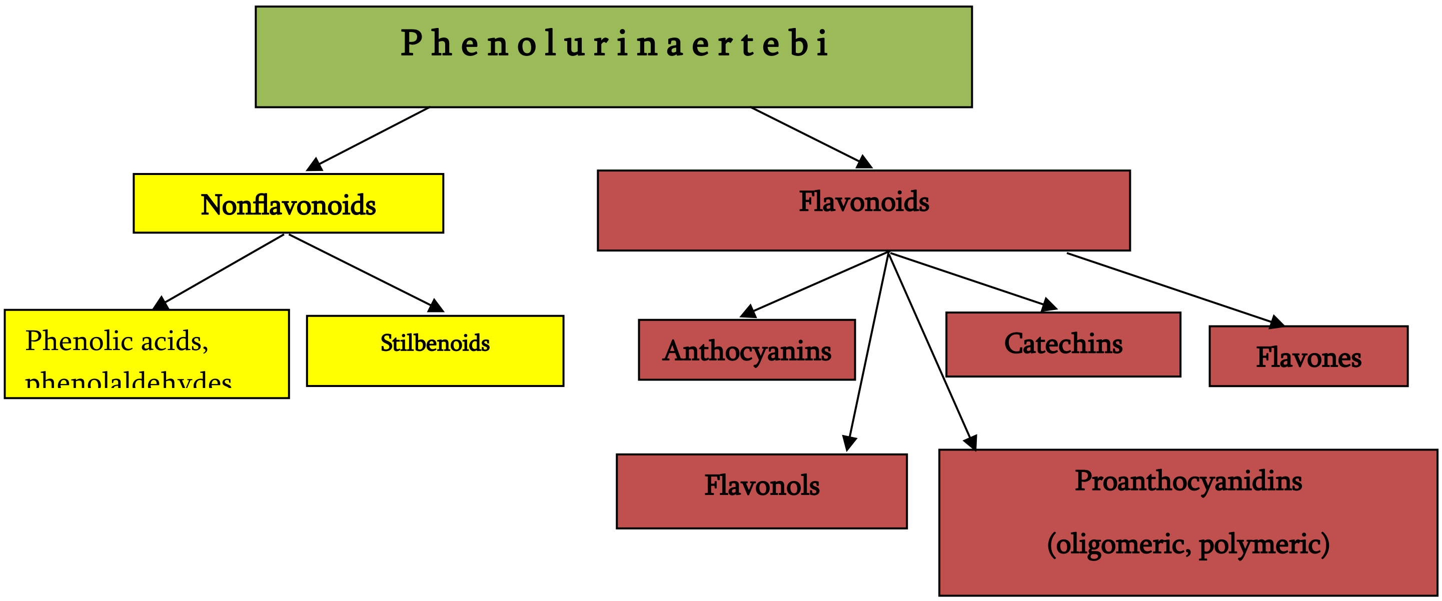
General characterization of grape and wine flavonoids and their biological activity

One of the determining factors of the quality indicators of wine is its chemical composition. The latter is represented in the form of grape components and their transformation products. The chemical components of grapes and wine are represented by various classes of compounds, of which phenolic compounds occupy an important place. The transformation of chemical components is characteristic of both the alcoholic fermentation of grape must and the formation of wine material. Phenolic compounds are transformed to some extent during the alcoholic fermentation of grape must and enrich the wine material with the corresponding products.

Phenolic compounds and their transformation products take an active part in shaping the quality of wine at all stages of its production and storage, and directly influence the taste, bouquet, color, transparency, stability , and shelf life. This explains the unwavering interest of researchers in studying these compounds.

It has been established that phenolic substances are the third most abundant chemical components in grapes after carbohydrates and organic acids. Flavonoids, which are components of phenolic compounds, are found in significant quantities in all parts of grapes: in the skin, in the pulp, in the pulp, in the juice, as well as in the juice. The total phenolic substances that are subject to extraction and are obtained from grape seeds are distributed as follows: 10% from the pulp, 60-70% from the pulp and 28-35% from the skin. However, it should be noted that a large number of phenolic compounds in the case of Cabernet Sauvignon grapes are localized in the skin of the grape (Prieur C. et al.,1994).

Phenolic compounds have been attracting the attention of researchers for almost a century, and this is evidenced by numerous scientific works that study the structure of phenolic compounds, the development and improvement of their research methods. The spectrum of phenolic compounds is rich and diverse. The composition of a wide class of grape phenolic compounds is presented in the form of a scheme (see Scheme 1.)



Scheme 1. Classification of grape phenolic compounds

The qualitative and quantitative composition of phenolic substances is different in red and white grape varieties. American scientists have established that in white grape varieties, phenolic substances are predominantly represented by coumaric acid esters, catechins and proanthocyanidins, including catechin gallate. In red grape varieties, phenolic compounds include hydroxybenzoic and hydroxycinnamic acids, proanthocyanidins, anthocyanins and glycosides of flavonols. The quantitative content of catechins in the pulp varies from 0.7-3.5%, in the skin 0.3-4.3%, in the seeds 2-3% (Ribereau-Gayon P.1964; 1994).

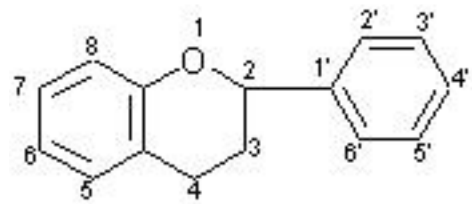
The authors determined the total amount of phenolic compounds, the quantitative content of catechins, proanthocyanidins, anthocyanins and their anti-radical effect in red and white wines made using Georgian traditional technologies, as well as in European-type wines. In particular, the total amount of phenols in Kakhetian-type white wines was 1330-2430 mg/l, while in Kakhetian-type red wines it was 2898-4416 mg/l, in European-type white wines it was 210-468 mg/l, and in red wines it was 1630-2340 mg/l (Shalashvili A. Et all.,2011).

The authors determined dihydroquercetin in wines from different countries: Moldovan wines contain - 0.5-2.4 mg/l; Georgian - 1.9-2.4 mg/l; French - 1.4-2.9 mg/l; Italian - 1.7-2.6 mg/l; Spanish - 1.4-2.2 mg/l; Chilean - 1.1-2.4 mg/l (Положникова М.А. et al.2005).

alcoholic fermentation of the grape varieties “Garnacha”, “Merlot” and “Syrah” (Aragon region, northeastern Spain) were studied. During alcoholic fermentation, high concentrations of anthocyanins, flavan-3-ols and flavonols were observed in “Syrah”: 802.7±0.5 mg/l; 74.7±2.4 mg/l and 37.1±1.5 mg/l (at the end of alcoholic fermentation, respectively). Overall, the results showed that the qualitative composition and concentration of phenolic compounds during alcoholic fermentation depend on the varietal factor (Puértolas E. , et al.,2011).

Phenolic compounds are contained in all parts of the vine in the form of monomers, polymers and oligomers. Phenolic acids, flavonoids (catechins, anthocyanins, leuco - anthocyanins, flavonols) and flavonoid polymerization products are considered to be the main phenolic compounds of grapes and wine and have been studied in depth (Durmishidze S. , Khachidze O. , 1985).

Flavonoids (C_6-C_3-C_6) (Latin : Flavus – yellow) are metabolic compounds of plant origin , which are derivatives of benzopyrone (chromone). Among the phenolic compounds, flavonoids are the most numerous. group . Currently , their number is known to exceed 8000. A flavonoid is an O - heterocyclic compound , the structural basis of which is a tricyclic molecule of flavone or flavan . The initial structure of flavonoids consists of two benzene rings connected by a three-carbon fragment , which together with an oxygen atom forms a pyrone ring . The benzene rings are denoted by the letters A and B of the Latin alphabet , and their connecting ring is denoted by the letter C. (Beecher GR, 2003; Gudvin T. И др., 1986; Barz W. Et all., 1975).



Basic structure of the flavonoid molecule

10 main subgroups according to the degree of oxidation of the three-carbon fragment , these are: catechins (flavan-3-ols), leucoanthocyanidins (flavan-3,4-diols), flavanones , dihydrochalcones , chalcones , anthocyanidins , flavonols and aurones . The diversity of -flavonoids is due to the hydroxylation , methylation , glycosylation of their molecules and the presence of asymmetric carbon atoms in the heterocyclic structure of flavanones , flavanonols , catechins and leucoanthocyanidins .

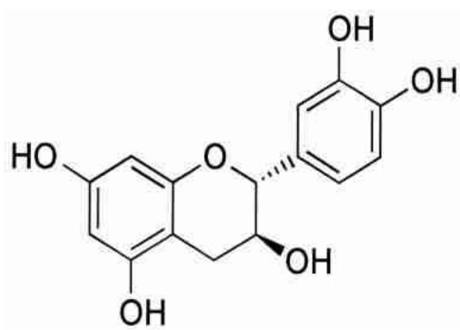
Among flavonoid compounds, catechins are the most abundant , while flavonols are the most abundant. Oxidized . Flavonones , catechins , and leucoanthocyanidins are colorless , flavones and flavonols are colored yellow , and anthocyanins have red , blue, and purple colorations (Navarri K. , Langlade F. ,2004)

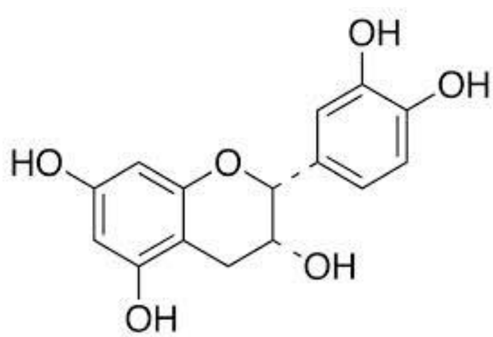
We considered it appropriate to present a brief chemical characterization of individual groups of grape phenolic compounds.

Catechins . Derivatives of 2-phenol-3-hydroxychrome belong to the subclass of catechins . These compounds have a close bond in the C2-C3 position and a C3 hydroxyl group. In their structure, there are two xyl centers with 2 and 3 carbon atoms. The well-known representatives include (+)-catechin and (-)-epicatechin . An important group of phenolic compounds in grapes and wine are catechins. In individual form, the following catechins are mainly found (Table 1; Brown J., et al.,2006).

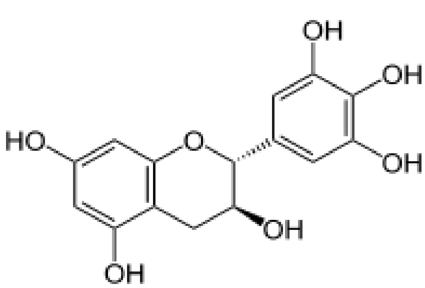
Table 1. Catechins of grape origin

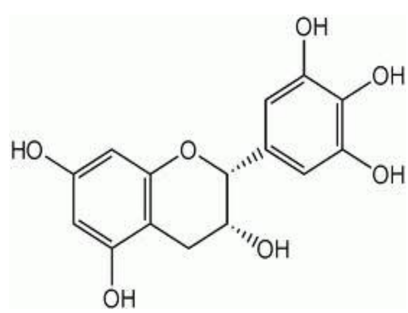
Flavanols	**R3**	**R1**	**R2**
(+)-catechin	H	OH	H
(-)-Epicatechin	H	H	OH
(+)-Gallocatechin	OH	OH	H
(-)-Epigallocatechin	OH	H	OH





(+)-Catechin $C_{15}H_{14}O_6$ (-)-Epicatechin $C_{15}H_{14}O_6$





(+)-Gallocatechin $C_{15}H_{14}O_7$ (-)-Epigallocatechin $C_{15}H_{14}O_7$

A significant part of grape flavonoids is made up of catechins . At present, catechins and their polymerization products are well studied among phenolic compounds. Catechins are colorless crystalline compounds. Methods for determining catechins are based on the presence of a phenolic oxy-group in their molecule, which gives qualitative reactions characteristic of phenolic compounds. It has been shown that catechins, when interacting with vanillin in a strongly acidic environment, give a pink color, and with ferric chloride - blue. In grapes and in products of its processing, catechins are found both in free and bound forms (Kishkovsky Z.N., 1976).

The content of catechins in different varieties of the grapevine "Vitis vinifera" was investigated. It was found that the qualitative composition of catechins in different parts of the grapevine is different , namely: all parts of the grapevine contain (+)-catechin, (±)-catechin is contained in the pith, skin, bract, stem, and is not included in the composition of the root. (±)-gallocatechin is included in the pith, bract, and skin, (+)-epicatechin gallate is a component of the pith, skin, and leaf. Other studies by scientists are consistent with the above results. Grape juice contains insignificant amounts of catechins, but as a result of processing with the Durdo enzymatic system, the amount of catechins increases sharply (Durmishidze S.V., 1954, 1955, 1958; Марх А.Т., 1969).

Catechins in grapes are present in the following proportions: (+)-catechin-50-100 mg/kg; (-)-gallocatechin-250-200 mg/kg; (+)-epicatechin gallate-40-500 mg/kg. The quantitative and qualitative composition of catechins in Rkatsiteli grape variety has been investigated. In particular, the following catechins were determined from the grape skin, skin and seeds during the period of full maturity: (+)-gallocatechin, (-)-epicatechin, (+)-catechin , (-)-epicatechin gallate (Durmishidze S. Khachidze O. , 1979; 1985; Gelashvili H.H., и др. 1970).

catechins have a pronounced bitter taste . Under the influence of oxidizing enzymes and as a result of heat treatment, the taste of catechins becomes soft and not sharp, with a pleasant bitterness , which is characteristic of high-quality wines (Durmishidze S. V. , 1955).

It has been established that the amount of catechins decreases during the wine maturation process ; in addition, (±) -gallocatechin decreases at the first stage of heat treatment . During 15 days of maturation, (+)- catechin decreases , and after 20 days and nights, only (-)- gallocatechin and (+)- catechin remain in the wine (Nutsubidze N.N., 1956).

According to the authors, the same catechins were found in dry red table wines made from Cabernet Sauvignon and Saperavi fermented on durdo as in grapes , except for (-)-epicatechin gallate. The amount of catechins in these wines was 247-250 mg / l . In those made according to the Kakhetian method , it was 600 mg / l (Valujko G. G., 1973) .

The amount of free catechins in wine decreases during the aging process, and in old wines their amount is completely absent. The same is confirmed by the data of other authors. In French wines, the amount of free catechins is up to 50-100 mg / l , while in wines aged for 3-4 years, there are no free catechins at all (Durmishidze S. V. , 1955; Ribero-Gayon J. and others 1980).

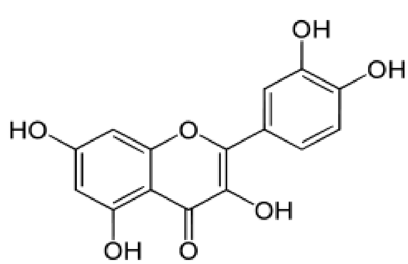
According to the currently available literature data, the main catechins in grapes are : (+)- catechin , (-)- epicatechin , (+)- gallo catechin , (-)- gallo catechin , (-)- epicatechin gallate. The qualitative composition and quantitative content of phenolic compounds in wines made in Kakhetian style in qvevri from autochthonous grape varieties of Georgia Velo, Tetri Rkatsiteli and Tsiteli Saperavi, have been studied . The following compounds were identified in wine made from Rkatsiteli grapes : (+)-catechin (32.6 mg/l), (-)-epicatechin (58.6 mg/l), (-)-gallocatechin (43.7 mg/l), in wine made from Saperavi grapes (+)-catechin (115.4 mg/l), (-)-epicatechin (29.5 mg/l), (-)-gallocatechin (174.4 mg/l) (Singleton VLet all.,1969; Shalashvili* A. et al. 2012).

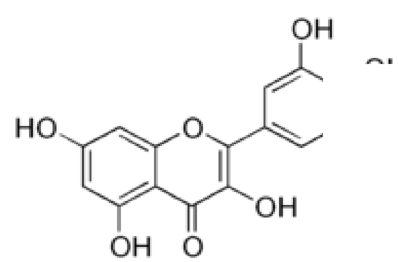
It is known that grape seeds are the richest in polyphenols among the hard parts of grapes. American scientists have established that (+)-catechin, (-)-epicatechin and (-)-epicatechin gallate (Edelmann A. et al., 2001; McDonald MS et al., 1998).

The difference in catechins contained in grape seed and grape skin tannins has been established. In particular, (+)-catechin , (-)-epicatechin predominate in grape skin tannins, while (-)-epigallocatechin, (+)-catechin predominate in grape skin tannins (Valujko G.G.,1973) .

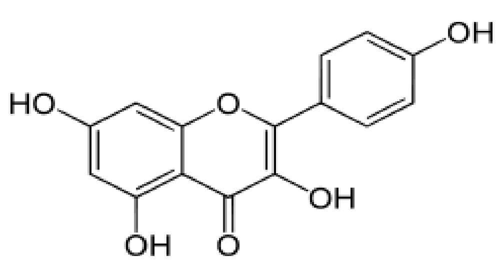
Flavonols. Flavonols are the most numerous and widespread group of flavonoids in the plant kingdom. They are yellow compounds. The flavonol group is a group of 2-phenyl-3-dihydroxychromone derivatives. They are distinguished from flavones by the presence of C3 hydroxyl groups. Representatives of this subclass are quercetin, morin, and myricetin. When discussing the structure of flavonoids, the main attention is paid to this subclass, since they are the most studied flavonoids with electron-donating properties (Brown JEet al.,2006).

Flavonols in grapes and wine are mainly present in the form of quercetin, myricetin, and kaempferol.





Quercetin $C_{15}H_{10}O_7$ Myricetin $C_{15}H_{10}O_8$



Kaempferol $C_{15}H_{10}O_6$

Quercetin-3-glucoside was first discovered in white grapes , and then kaempferol, myricetin and their glycosides were discovered. The main flavonol in grapes is quercetin-3-glucoside (isoquercitrin), the amount of which is 56-58% of the total amount of flavonols. In different grape varieties, flavonols are present in the form of glycosides and the main aglycones - quercetin, kaempferol, myricetin, isorhamnetin. Phyllium was isolated from various parts of grapevines distributed in Georgia and both aglycones and glycosides of flavonols were identified: kaempferol, kaempferol-3-glucoside (astragalin), quercetin, quercetin-3-rhamnoside (quercitrin), quercetin-3-glucoside (isoquercetin), quercetin-3-rutinoside (rutin), quercetin-3-glucuronide, myricetin, myricetin-3-glucoside (Durmishidze S. Khachidze O. , 1979, 1985; Edelmann A. et al., 2001; Valuyko G.G., 1973).

Red Spanish wines made from Tempranillo, Graziano, Cabernet Sauvignon and Merlot grapes contain flavonols: myricetin-3-0-glucuronide 1.57-4.69 mg/l, quercetin-3-0-glucuronide 1.3-8.5 mg/l, myricetin 1.33-3.15 mg/l, quercetin 1.88-6.90 mg/l, kaempferol-3-0-glucoside (not present in Merlot) - 1.23-2.03 mg/l; quercetin -3-0-galactoside was found only in Cabernet Sauvignon - 1.05 mg/l. Myricetin-3-glucoside, quercetin-3-glucoside, rutin , myricetin, quercetin, hesperidin, and kaempferol have been identified in wines (Sun Y. et al.,2007; Yustesen U. Et al.,1998).

The quercetin content of Georgian table red wines made from Saperavi grapes varies - depending on the region and ranges from 0.9 to 2.78 mg/l. The total flavonol content of wines made from the Kakhetian Rkatsiteli grape variety in different regions of Kakheti is 22.0 to 42.0 mg/l. Red wines made in different countries contain 0.16 to 1.77 mg/l of quercetin and 0.18 to 2.20 mg/l of myricetin, while the total flavonol content of red wines (quercetin+myricetin+kaempferol+isoramnetin) is: Cabernet Sauvignon (Chile) - 58.4 ± 4.0 mg/l; Pinot (California) - 30.2 ± 0.6 mg/l; Merlot (Chile) - 25.2 ± 1.2 mg / l; Biojolais (France) -

9.9 ± 0.9 mg / l; white wine Riesling (Australia) contains 1.7 ± 0.2 mg / l of the above-mentioned flavonols, while in other white wines they are not observed (Bezhuashvili M. and others, 2005; GrozierA. GrozierA.,,et al.,2000; Daniel O.et al.,1999).

It has been established that red grape varieties contain more flavonols than white varieties, and at the same time, the content of flavonols in different parts of the grape differs from one another. It has been found that all the hard parts of the grape contain quercetin, quercitrin and isoquercitrin. Two aglycones - quercetin and myricetin, glucosides - quercitrin, isoquercitrin and myricetin-3-glucoside were found in the skin of Saperavi and Matrasa grapes. Glucosidic flavonols were isolated in the skin of red grapes : kaempferol-3-glucoside, myricetin-3-glucoside-15%, quercetin-3-glucoside-50%, quercetin-3-glucoside-30%. The quantitative content of flavonol aglycones and glucosides in red and white wines was determined (Ribereau - Gayon P. , 1964; Bokuchava M. et al., 1971; Sturua Z. et al., 1971; Rodopulo A., 1971).

Flavonols were identified in wines made from Saperavi grapes and aged in Kakhetian qvevri: kaempferol (13.2 mg/l), quercetin (11.2 mg/l), rutin (2.6 mg/l) (Shalashvili A. et al., 2012).

Alcoholic fermentation of grape must is the main stage in the production of Kakhetian and Imeretian-type wines, which is characterized by the enrichment of wine materials with phenolic compounds - in natural form and their transformation products. Phenolic compounds accumulate in the process of alcoholic fermentation both in natural and transformed forms. The effect of wine yeasts on flavonols was studied and the path of flavonol transformation was identified (Shoniya T. Bezhuashvili M. et al., 2006, 2008,2009).

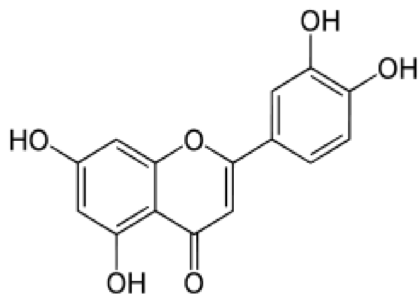
The study was conducted on white wines, specifically two white grape varieties were used: “Arinto” and “Muscatel”. The “Arinto” variety showed higher concentrations of quercetin-3-glucoside and kaempferol-3-glucoside than the “Muscatel” variety (Alexandros D.et al.,2005) .

Individual representatives of flavonols have been identified in red wines produced from several red grape varieties in different countries (see Table 2).

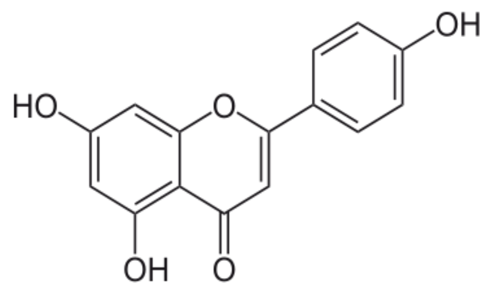
Table 2. Flavonol content (mg/100ml) in red wines

Grape variety	Country	Year	Quercetin	Myricetin	Kaempferol
Cabernet Sauvignon	Australia	1994	1.73	1.76	0.21
,,-------,,	,,-------,,	1995	1.59	1.00	-
,,-------,,	Bulgaria	1995	0.16	0.29	-
,,-------,,	Chile	1994	1.77	1.80	-
,,-------,,	France	1992	0.69	1.49	-
,,-------,,	,,-------,,	1994	1.24	2.20	-
,,-------,,	Spain	1993	0.76	1.52	-
,,-------,,	USA	1994	0.93	1.23	-
Agiorgitiko	Greece	1994	0.84	0.47	-
Merlot	Chile	1994	1.28	1.82	0.13
,,-------,,	France	1994	1.41	1.52	0.08
Pinot Noir	,,-------,,	1991	0.25	0.18	-
Nebiol	Italy	1990	0.90	0.47	-
,,-------,,	,,-------,,	1992	0.60	0.25	-
Sangiovese	,,-------,,	1994	0.60	0.52	0.08
,,-------,,	,,-------,,	1995	0.71	0.52	-
Tempranillo	Spain	1993	0.17	0.46	-
Mixture	France	1992	0.91	1.72	-

Flavones. Flavones are found in plants both as aglycones and as glycosides. More than 40 aglycones of flavones are known today, the main ones being: apigenin, luteolin, tricin. Apigenin and luteolin have been found in grapes as glycosides of flavones.



Luteolin $C_{15}H_{10}O_6$



Apigenin $C_{15}O_{10}O_5$

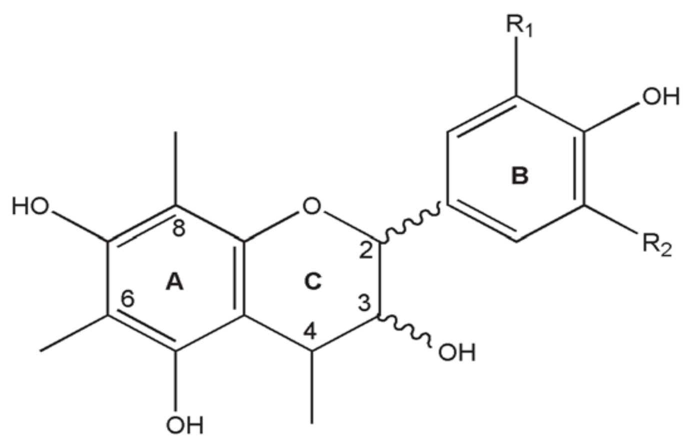
Flavones form glycosides of the O and C types, this latter being more characteristic of them than of other flavonoids. Among the O-glycosides of flavones, the most important are 7-0-glycosides and 7-0-rutinosides; 5-diglucosides are also known (Durmishidze S. Khachidze O. , 1979).

Saperavi, Rkatsiteli, Marsala and other grape varieties (leaves, shoots, annual stem, stamens, inflorescence, grape skin, claret), luteolin-glucoside was identified. An apigenin derivative was also found in grapes (Durmishidze S. Khachidze O. , 1985).

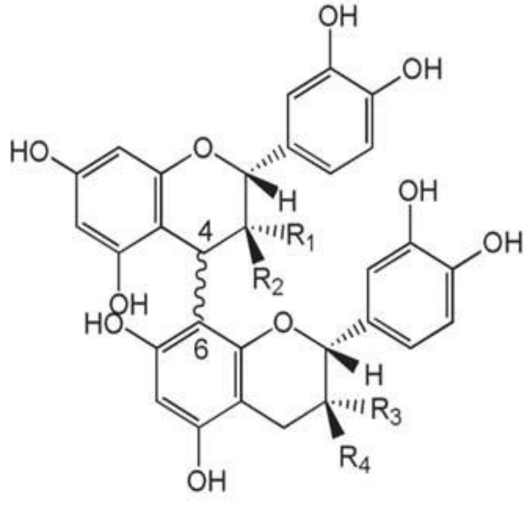
Proanthocyanidins. Proanthocyanidins (leuco anthocyanins) or flavan-3-4-diols are important phenolic components. These compounds have a great influence on the quality of wine both from an organoleptic point of view and from a therapeutic and prophylactic value. Proanthocyanidins are a source of condensed tannins. Proanthocyanidins form anthocyanidins when heated in an acidic environment in the presence of oxygen. Low-molecular procyanidins have less pronounced tanning properties and do not stain proteins. With an increase in the degree of polymerization of proanthocyanidins, their tanning properties increase. Dimeric, trimeric, tetrameric and polymeric forms of proanthocyanidins are found in red wine , among which the polymeric form predominates. The amount of leucoanthocyanins in table wines made from Saperavi grapes distributed in the Kakheti region is: 1.72-2.65 g/l. The minimum -

1.72 g/l was recorded in the wine materials of the Akhmeta region, and the minimum - 2.65 g/l in the wine materials of the Khashmi microdistrict (Kvlividze D. , Bezhuashvili M. , 2005).

Five different dimers have been isolated from red wine: B1 , B2 , B3 , B4 , B5 , and two trimers. These dimers and trimers represent condensed catechins and epicatechins (Weinges K. et al.,1971; Powell H. et al.,1987; Santos-Buelga C.et al.,2000).



Basic structure of proanthocyanidin: R1, R2=H (propelargonidin); R1=H, R2=OH (procyanidin); R1,R2=OH (prodelphinidin)



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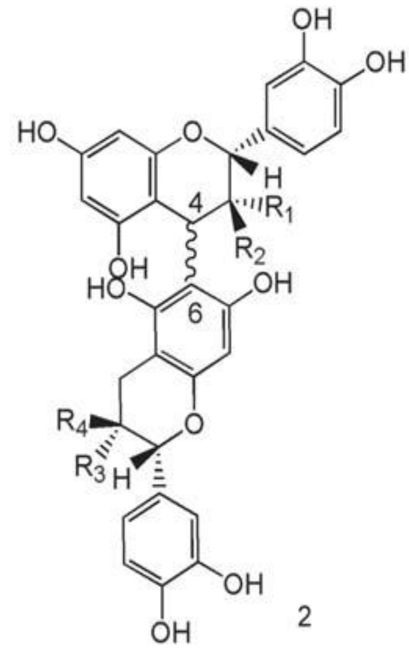

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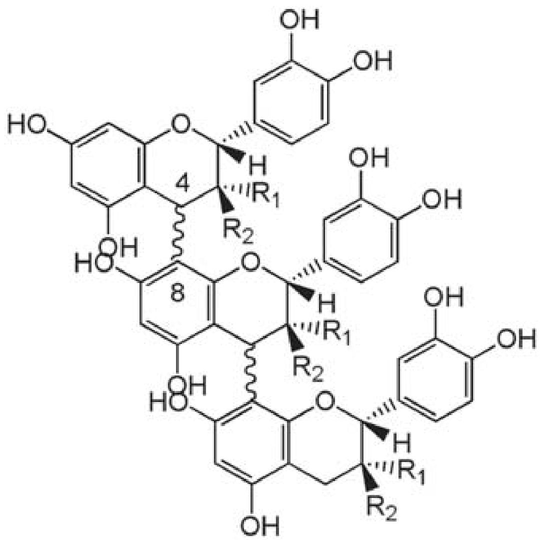

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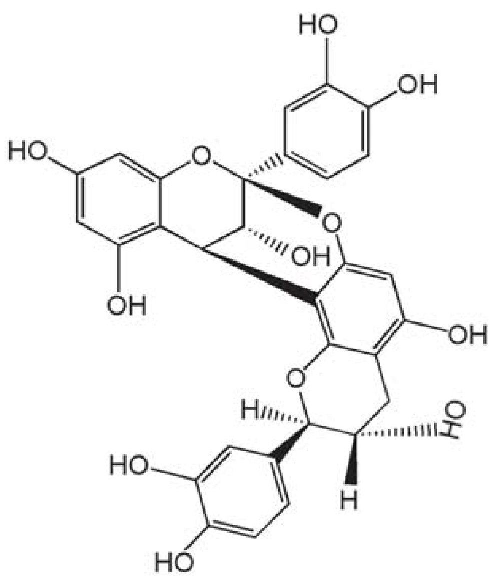

4

Structure of some A, B, C type proanthocyanidin dimers and trimers

1 – B1 : R 1 =OH; R 2 =H; R 3 =H; R 4 =OH; **B2** : R 1 =OH; R 2 =H; R 3 =OH; R 4 =H; **B3** : R 1 =H; R 2 =OH; R 3 =H; R 4 =OH; **B4** : R 1 =H; R 2 =OH; R 3 =OH; R 4 =H;

2 – B5 : R 1 =OH; R 2 =H; R 3 =H; R 4 =OH; **B6** : R 1 =H; R 2 =OH; R 3 =OH; R 4 =H; **B7** : R 1 =H; R 2 =OH; R 3 =H; R 4 =OH; **B8** : R 1 =H; R 2 =OH; R 3 =H; R 4 =OH;

3 – **C1** : R 1 =OH; R 2 =H; **C 2** : R 1 =H; R 2 =OH;

4 – **A2**

red grape varieties common in Georgia contain both oligomeric and polymeric proanthocyanidins. Their amounts are as follows: Saperavi dry wine: oligomeric-988 mg/l, polymeric-3200 mg/l; Cabernet dry wine: oligomeric-892 mg/l, polymeric-2050 mg/l; Otskhanuri Sapere dry wine: oligomeric-992 mg/l, polymeric-3000 mg/l; Ojaleshi naturally sweet wine: oligomeric-044 mg/l, polymeric-1455 mg/l; Aladasturi dry wine: oligomeric-364 mg/l, polymeric-1950 mg/l; Alexandroupoli naturally sweet wine: oligomeric-807 mg/l, polymeric-1235 mg/l; Mujuretuli naturally sweet wine: oligomeric-972 mg/l, polymeric-1365 mg/l; Chkhaveri pink wine: oligomeric-936 mg/l, polymeric-1200 mg/l (Vepkhishvili N., Vezhuashvili M. et al. 2010).

It has been established that in red wines made from technical grape varieties, oligomeric proanthocyanidins are significantly lower than polymeric proanthocyanidins, while in wines made from direct-producing hybrid forms, the opposite is true. The same authors presented this difference as an indicator of varietal purity in Georgian red wines, and the ratio K=opc/ppc represents an indicator of varietal purity of red wines made from technical varieties (Bezhuashvili M., Deisadze I. et al., 2008).

Oligomeric proanthocyanidins are water-soluble substances. They undergo hydrolysis in acidic and alkaline environments. During the alcoholic fermentation process, they are intensively extracted from the skins and localized in the wine material. Scientists have investigated the amount of polymeric and oligomeric proanthocyanidins and catechins transferred from the hard parts of grapes (seeds, skins, and claret) to red wine as a result of fermentation. The concentration of proanthocyanidins and the range of polymer content were investigated in the seeds and skins of the Cabernet Sauvignon grape variety grown in Australia and in Shiraz wine (SunB. Et al., 1999; Hanlin R. Et al.,2011).

made from Saperavi grapes distributed in the regions of Kakheti is: 1.72-2.65 g/l, the minimum - 1.72 g/l was recorded in the wine material of the Akhmeta region, and the maximum - 2.65 g/l in the wine material of the Khashmi microdistrict (Kvlividze D. , Bezhuashvili M. , 2005).

Oligomeric proanthocyanidins were determined in Spanish, French and some American red wines; in Spanish (Tempranillo - from the 1995 harvest) dimeric proanthocyanidins - 83.77 mg/l, trimeric - 26.98 mg/l, tetrameric - 21.17 mg/l; in French (Cabernet Sauvignon from the 1997 harvest) dimeric - 214.60 mg/l, trimeric - 30.17 mg/l, tetrameric - 42.42 mg/l; In American (Château-Chateaunet from the 1997 harvest) dimeric - 27.90 mg/l, trimeric - 11.14 mg/l, tetrameric - 5.38 mg/l (Sánchez -Moreno C.et al.,2003).

determining proanthocyanidins in Spanish red wine, only the dimeric B_1 and B_2 forms were detected in the following amounts: in Tempranillo B_1 -7.10±0.08 mg/l, B_2 -7.40±0.13 mg/l; in Graziano B_1 -15.96± 0.02 mg/l, B_2 -17.5±0.95 mg/l; in Cabernet B_1 -11.21±0.56 mg/l, B_2 -15.31±0.28 mg/l; in Merlot B_1 -4.96±0.07 mg/l, B_2 -6.97±0.13 mg/l (Monagas M . Et al.,2005).

American scientists have established that grape seeds also contain a large amount of dimeric flavan-3-ols, which are called proanthocyanidins. The latter are slowly broken down by acid hydrolysis to form cyanidins. Five dimer proanthocyanidins have been isolated from red wine: (B1, B2, B3, B4, B5) and two trimers. These dimers and trimers are condensed products of catechin and epicatechin (Valuyko G., 1973; Su T., et al., 1969; Weinges K. Et al., 1971).

The study of the biological activity of phenolic compounds is a current research direction. Due to the rich phenolic composition of grapes and wine, studies in this direction have added considerable importance to the scientific foundations of winemaking.

The study of the biological activity of flavonoids began in the 1930s. However, interest in flavonoids continues to this day. For a long time, it was believed that the biological activity of phenolic compounds lies in their antioxidant activity and that they have the ability to react with free radicals, which manifest themselves under conditions of oxidative stress. Recently, it has been established that flavonoids can influence signaling processes that occur in living systems due to the specific action of proteins that perform regulatory functions. The high antioxidant activity of phenolic compounds is widely used in practice for the prevention and treatment of diseases (Benthsath A., 1936; Middleton E.,2000; Willcox JK,2004; Soobrattee MA,2005; Stevenson DE, 2007; Khavinson V. Kh.,2003; Singh M.,2008).

According to the literature, flavonoids have the ability to react with free radicals. This property is of great interest, since it is the basis of the antioxidant activity of phenolic compounds. As a rule, the action of flavonoids on free radicals proceeds rapidly, resulting in the inactivation of radicals. It is believed that when interacting with radicals, a phenolic substance can act as a proton donor (1) or as an electron donor (2) (Kostyuk V. A. and others, 2004, Seyoum A., 2006; Kandaswami C. et al., 1994; Wright JS, 2001).

$$PhOH + R^{\bullet} \rightarrow PhO^{\bullet} + RH \quad (1)$$

$$PhO^{-} \rightarrow PhO^{\bullet} + e^{-} \quad (2)$$

Which reaction will proceed depends on the structure of the flavonoid, the nature of the free radical, and the conditions of the reaction. In both cases, the initial flavonoid is transformed into the same intermediate product ($PHO^{\bullet}$), which is called the phenoxy radical. It is a highly unstable compound that is rapidly transformed into various derivatives of the initial flavonoid or enters a new cycle of oxidation-reduction reactions. The reactivity of the phenoxy radical, the structure of the products into which the initial flavonoid has passed, is also determined by the nature of the initial flavonoid itself and the conditions of the reaction. Flavonoid oxidation intermediates that contain a catechol group and one extra electron in their structure are called semiquinones, while those that contain two electrons are called quinones, respectively (Jovanovic SV, 1994 ; Fiorucci S., 2007).

The spectrum of radicals with which flavonoids can interact is quite wide. Flavonoids are able to react with both organic and inorganic free radicals. The inorganic group includes the interaction of nitrogen dioxide and superoxide anion with hydroxyl radical. These compounds are formed in large quantities when the functioning of oxidative metabolism enzymes is disrupted, which can lead to a fatal outcome for the entire organism (Kostyuk V. et all.,1989; Wilms LC,2008; Papa S. Et al.,1997).

the superoxide anion-radical reaction of flavonoids is currently considered to be well established. Its essence (3) is as follows:

$$PHO^{-} + O_2^{\bullet} \rightarrow PHO^{\bullet} + O_2^{2-} \quad (3)$$

It has been found that the most effective superoxide scavengers are the flavonols rutin and quercetin. These substances have a free catechol group in the B ring, and as scientists indicate, the reaction with the superoxide anion radical occurs precisely at the expense of hydroxyl groups (Jovanovic SV, 1994).

Flavonoid oxidation occurs in both plants and animals. For plants, this process is an important stage for normal growth and development. For example, flavonoid oxidation is observed during seed ripening. As a result, polymeric compounds are formed on the surface of the seed coat, which causes its coating to darken and at the same time reduces water permeability. The oxidative transformation of flavonoids consumes intracellular oxygen and water, which protects the seeds from damage. This fact is very important when conducting selection work. The use of plants with a high content of flavonoids can contribute to the production of varieties that differ in a long storage period of seed material. Flavonoid oxidation in plants occurs not only under normal, but also under stressful conditions. During the development of fungal and bacterial infections, a high level of quercetin oxidation is observed, resulting in the formation of 3,4-dihydroxybenzoic acid, which has fungicidal and bactericidal activity. Physiological damage to plant tissue causes the process of oxidative degradation of flavonoids, which prevents the development of early infections. It is noteworthy that during the development of roots, on the surface of cells that actively interact with the environment, there is a significant amount of phenols that protect plants from pathogens. The protective properties of flavonoids and their oxidized derivatives are manifested not only by binding pathogens, phenolic substances participate in the utilization of the active form of excess oxygen. The path of development of phenolic substances and the possibilities of detecting their biological activity are still the basis for active discussion today (Pourcel L.,2007; Egley GH,1985; Bailly C.,2004; Aziz NH,1998; Walker JR Et all., 1998; Rahman M. Et all.,2005; Feeny PP,1974; Walle T.,2004).

Until now, it was believed that flavonoids limit the development of oxidative stress by accompanying redox reactions. By similar mechanisms, they increase the stability of many biologically important compounds, such as ascorbic acid and carotenoids. It has been established that flavonoids are distinguished by antiallergic, anticarcinogenic , antiviral and anti-inflammatory properties (Clemetson CAet all.,1966; Korkina LG,2008).

Flavonoids in plants perform ecological functions - antiradiation and antibacterial. Quercetin is characterized by antimicrobial effect, antiviral and antioxidant activity, cardioprotective and antiplatelet activity (Stavric B.,1994; Vrijsen R.et al.,1998; Бежуашвили М.Г. и др.2005; Conquer YA et al.,1998; Takahama U., 1985; Pace-Asciak CRet all.,1995).

Red wines have higher antioxidant activity than white wines, which is due to the difference in the qualitative and quantitative composition of phenolic compounds. One study found that among South African wines, “Pinotage” wine stands out, which has a unique phenolic profile and, therefore, is characterized by optimal antioxidant activity while maintaining good organoleptic properties (De Beer, D. et al., 2003).

Changes in conventional and organic wines during 7-month storage were studied. The content of polyphenols and free radicals was determined. The most variable component in red wine during storage was found to be anthocyanins, as the content of anthocyanins decreased significantly in conventional and organic wines during storage. In contrast to other studies, the total concentration of phenolic compounds in conventional and organic red and white wines was not related to antioxidant activity. No significant difference in antioxidant activity was observed in red wine between organic and conventional wines, but at the same time, a significant difference in antioxidant activity was observed between conventional and organic white wines (Zafrilla P.et al.,2003).

Six white wines and two red Greek wines were evaluated for their ability to inhibit low-density lipoprotein oxidation. All red wines were found to have higher antioxidant activity and total phenolics than white wines.

Young and aged wines were also compared. Young wines differ from aged wines in relevant components, indicating that oxidative aging in barrels may affect the antioxidant potential of wines. All of these active wine fractions are rich in phenolic acids and flavonols (Alexandros D.et al.,2005).

A number of studies have been conducted on red, white and rosé wines in Europe and America to assess their antioxidant capacity, but this is the first study on South African wines. The free radical scavenging potential of the red wines Pinotage and Merlot was highest (15-15) and Cabernet Ruby was lowest (13). In the lipid peroxidation assay, Merlot and Cabernet Ruby had the highest and lowest activity, respectively (75-55). The white grape wine "Chardonnay" showed the highest (1.1-70) and "Chenin Blanc" the lowest (0.8-38) activity in the free radical and lipid peroxidation test, while "Sauvignon Blanc" and "Colombard" wines had intermediate antioxidant activity (0.9-49), (0.9-40) (102,104-107 - De Beer D. et al., 2003, 2005; Campos A. et al.,1996; Simonetti P. et al.,1997; Landrault N. et al.,2001).

Flavonoids are natural antioxidants found in fruits, vegetables, wine, tea, and other foods. Flavonoids have been shown to reduce the oxidation of low-density lipoproteins, which can lead to a reduced risk of blood clots. Scientists have studied the effects of quercetin, kaempferol, myricetin, apigenin, and luteolin on the human body, particularly on the risk of coronary heart disease. The study subjects were men aged 65 to 84 who consumed 259 mg of flavonoids daily in the form of tea, onions, and apples. Of the 693 subjects, 38 had a myocardial infarction. An experiment found that regular consumption of foods rich in flavonoids reduces the risk of death from coronary heart disease in older people, even after controlling for weight, tobacco and coffee consumption, cholesterol, blood pressure, and physical activity (108 - Bertelli AF,1995).

The biological activity of flavonols, flavones and anthocyanins, their antioxidant properties and positive role in reducing the oxidation of lipoproteins have been established. Quercetin , kaempferol, myricetin, apigenin and luteolin protect the human body from blood clots and cholesterol and reduce the risk of heart disease even in conditions of high blood pressure. Most diseases are caused by the excess of oxygen on the tissue . In this case, some flavonoids, e.g. quercetin and silibinin, effectively protect cells and tissues from the harmful effects of oxygen. Their antioxidant properties are manifested by binding free radicals and other intermediate oxidants. The antioxidant activity of pH-dependent forms of anthocyanins in Georgian red wine made from Saperavi was determined in in vitro experiments as the degree of inhibition of malondialdehyde formation in human blood (Bezhuashvili M. G. et al., 2005).

The authors' studies showed that the consumption of quercetin and catechins reduces the development of atherosclerosis in mice, which is due to a reduced sensitivity to lipoprotein oxidation. The studies showed that flavonoids in red wine - natural antioxidants - inhibit the oxidation of low-density lipoprotein. As a result of this experiment, the oxidation of low-density lipoprotein decreased by 45%. In healthy people who consumed 400 ml of red wine per day, the degree of oxidation of low-density lipoprotein significantly decreased for 2 weeks.

As a result of studies conducted in Chile in 2002, scientists determined the effect of quercetin, myricetin and catechin gallate on glucose transport. Simple and facilitated glucose transporters are membrane proteins that are responsible for the transport of hexoses across the plasma membrane. One such transporter is the so-called "GLUTU". The translocation of the latter across the plasma membrane is regulated by insulin. When there are abnormalities - accumulation of fat in the abdominal area, in this case, the disruption of insulin-induced signaling leads to the translocation of "GLUTU" and the associated disruption of glucose metabolism. The positive effect of the above-mentioned flavonoids on the transport activity of

"GLUTU" was established by model experiments. Researchers from the University of California studied the inhibitory effects of (-)-epicatechin, (+)-catechin, and dimeric procyanidins on NF-κB-mediated T cell activity. Wine flavonoids were identified as peroxynitrite scavengers. Three main types of free radical reactions occur in the human body: in the blood vessels, in the intestine, and in the subcellular space. The main pathway is the same in all three cases, but the initiating processes and participating antioxidants are different. The intravascular reaction is initiated by plasma ONOO and the radical. The radical is formed on the surface of low-density lipoproteins and the process is catalyzed by metal-containing (Fe, Cu) plasma proteins. Flavonoids in this process exhibit high antioxidant activity in the form of free radical oxidation. Red wine containing flavonoids, about 1 glass per day, reduces oxidative processes by 50% in in vitro experiments. Plasma triglycerides and radicals increase during the period of eating. Flavonoids (0.5 g/day) cause an antioxidant effect in the intestines, which is 5-10 times higher than the antioxidant effect of vitamins C and E. It has been proven through nutrition that red wine and flavonoids significantly reduce postprandial oxidative stress inside the blood vessels.

The bactericidal effect of red wine was investigated, for which its antimicrobial effect was compared with bismuth salicylate. The purpose of this experiment was to explain the legendary reputation of wine as a digestive system regulator. Researchers in Northern California determined the relationship of the risk of coronary heart disease to red and white wines. The trial was conducted in hospitalized conditions on 934 men and women. The predominant positive effect of red wine on heart disease was established in both sexes (Weisse MEet al.,1995; Klatsky A. Et al.,1997).

According to a number of scientists, the cardioprotective effect of red wine is mainly due to the antioxidant activity of resveratrol and quercetin (Constant J.,1997; Jarret.N.et al.,1997; 47
Grande l.et al.,1997).

Studies conducted in France have shown that the risk of breast cancer is limited by the consumption of red wine (4 liters per month) (Viel J et al., 1997).

, which confirms the medicinal and nutritional values of wine, demonstrate without any doubt the medicinal effect of wine in reducing the risk of cardiovascular diseases, carcinogenesis, diabetes, mental illnesses, the development of metabolic syndrome, improving bone strength, protecting against asthma attacks and other diseases.

Based on the literature, a large number of studies have been clearly demonstrated, which are devoted to the so-called "French paradox" phenomenon, which, in addition to its nutritional value, gives red wine a large and diverse therapeutic load. The dose established by scientists is considered to be 200-300 ml of red wine per day for a healthy male, and 100-200 ml for healthy women (Lugasi A.et al.,1997; Kondo K.et al.,1994; De Rijke YBet al.,1995; Frankel ENet al.,1993).

In vitro studies from the Department of Medicine at the University of Western Australia have shown that red wine, and in particular the phenolic acids isolated from wine, have significant antioxidant activity (Abu-Amsha-Caccetta R.,2001; Caccetta RA,2000).

Studies show that regular consumption of certain plant-based products reduces the development of atherosclerosis and atherothrombosis in humans. These studies were conducted in 1985 in the Netherlands. 805 men aged 65 to 84 years participated in them, who were followed for 5 years. The authors tried to answer the question of whether the use of vegetables, fruits, and beverages containing flavonoids (quercetin, kaempferol, myricetin, apigenin, luteolin) in food affects the risk of coronary heart disease and myocardial infarction. It turned out that in addition to the risk of developing coronary heart disease, the risk of death from coronary heart disease was significantly higher with a daily intake of up to 19 mg of flavonoids than with a daily intake of more than 30 mg of flavonoids. I.e. A relatively high level of flavonoid consumption reduces the risk of developing these diseases. Studies have shown the importance of flavonoids in the prevention of cardiovascular diseases (Maslova L.N., 2007).

Plant-derived phenolics have been reported to have various biological effects, including antioxidant , anticarcinogenic, anti-inflammatory, and antimicrobial activities. In particular, some phenolic compounds, such as resveratrol, quercetin, and a number of phenolic acids, have been reported to inhibit various pathogenic organisms. In addition, there are studies on the antimicrobial activities of wine and wine extracts on pathogenic microorganisms (Chan MMY. , 2002; Daroch F. , 2001; Feringa HHH, 2011)

Grape skin and seed extracts have great potential in cancer prevention and are being studied in this direction. A growing number of epidemiological studies and human controlled trials have linked the widespread consumption of grapes, grape juice, and wine to improved health, specifically the risk of cardiovascular disease, type 2 diabetes, various types of cancer, and other chronic complications (Mellen P., et al., 2010; Kar P ., et al.,2009; Castilla P., Dávalos A., et al., 2008; Castilla P.,Echarri R., et al., 2006; Brooker S., et al., 2006; Preuss HG, et al., 2000).

Flavonoids have diverse pharmacological actions in the central and peripheral nervous systems. However, flavonoids can exert even more diverse actions on cellular signaling mechanisms, for example, the green tea polyphenol (-)-epigallocatechin-3-gallate, which can exert multiple effects on intracellular life (BASTIANETTO S., et al., 2000; JIANG F., et al., 2003; (MANDEL S., et al., 2003).

Nutrients such as vitamin E, vitamin D, green tea and wine polyphenols have been shown to inhibit the proliferation of prostate cancer cells in cell lines. Polyphenols may have anti- proliferative effects. They may prevent the spread of prostate cancer (Romero I., Paez A., Ferruelo A., lujan M. Berenguer A. 2002).

Due to the versatile biological activity of bioflavonoids, they can be used in cosmetic products as a means for sensitive skin, anti- cellulite, anti-premature aging, etc. (Локацкая . 2007).

Bioflavonoids are widely distributed substances in plant tissue. The antioxidant and antimicrobial activity of flavonoids has been demonstrated . The important role of flavonoids in diseases such as cardiovascular diseases, cancer, various inflammatory processes and allergic diseases has been confirmed . Flavonoids have been investigated for their antioxidant activity during lipid oxidation, in particular, in low-density lipoproteins and liposomes. In addition to antioxidant properties, bioflavonoids are characterized by antiallergic activity. Quercetin, rutin, cyanidin are distinguished by the most pronounced antiallergic activities. Bioflavonoids are also characterized by anti-inflammatory properties, they inhibit inflammatory processes (Yao, L. et al., 2004; Ferguson, PJ et al.,2004; Havsteen, B., 1983; Lyons-Wall, PM et al., 1997; Ma, TE et al., 2004; Moon, YJ et al., 2006; Duan, XW et al., 2007).

Scientists have determined that the following individual substances exhibit P-vitamin activity: rutin, quercetin, isoquercetin , (+)-catechin, (-)-gallocatechin, unoxidized wine tannin, and anthocyanins (Edelmann A., Diewok J., Schuster K. S. , Lendl. V. , 2001; Cossins E. , Lee R., Packer L., 1998).

The effects of quercetin, myricetin, kaempferol, apigenin and luteolin on the human body have been studied. In particular, their role in preventing the risk of death from coronary heart disease has been established. The antioxidant and antitumor activity of quercetin and kaempferol is known. The effects of quercetin and its metabolites in the body on non-cellular liver extracts have been studied. It has been confirmed that their biological activity depends on the distribution and concentration of quercetin in plasma (Hertog MGL, 1995; Day AJ, Bao Y., A Morgan MR, Williamson G. 2000).

It has been proven that the consumption of quercetin and catechins reduces the development of atherosclerosis in mice, which is due to a decrease in the oxidation of lipoproteins. It has also been proven that catechins can prevent Fe^{++} and Gu^{++} lipid - peroxidation in low-density lipoproteins. Catechins restore blood microcirculation, improve the elasticity of blood vessels, have hypocholesterolemic and antiatherosclerotic effects. The P-vitamin activity of catechins at equal concentrations is 2 times greater than that of rutin. Catechins increase the resistance of the walls of blood-carrying arteries, thereby promoting the absorption of ascorbic acid by the body (Cossins E., Lee R., Packer L., 1998).

Research Objective: The research objective was to determine the variability of flavonoids in the red grape wine grape variety Chkhaveri under conditions of vineyard soil treatment with a biostimulant.

Research objects. The research objects were biostimulant-treated and untreated grape skins taken from the Chkhaveri vineyard, a red grape wine grape variety grown in the village of Zemo Bakhvi, Ozurgeti district, western Georgia.

Research methods. We treated the soil of the Chkhaveri vineyard with a biostimulant in the spring of 2023. We harvested grapes from both the control and experimental variants during the period of technical ripeness.

We determined the sugar content in Chkhaveri grape juice using a special hydrometer. We separated the grape skin from the grape seeds, dried it at room temperature, crushed it and used it to determine proanthocyanidins, total phenols, catechins, and anthocyanins. We determined the total phenols in the grape skin using the Folin-Chocolate reagent by spectrophotometric method. The determination was carried out at a wavelength of 700 nanometers (Sederi, Datunashvili, 1970). Phenolic substances were extracted from the grape skin by hot extraction with ethyl alcohol. Anthocyanins were extracted from the grape skin by hot extraction with 80% ethyl alcohol acidified with hydrochloric acid. The determination was carried out at a wavelength of 520 nm. Catechins were determined spectrophotometrically at a wavelength of 500 nm according to the appropriate method (Valuiko G., 1973). The total amount of flavonols was determined by converting to quercetin, spectrophotometrically at a wavelength of 415 nm (Anda Patanela Crosi, 2009) . The concentrations of the above substances were calculated using special calibration curves.

Research results.

Table. Variation of flavonoids in Chkhaveri grape skins as a result of bioactivator treatment

N	Flavonoids	Control-unprocessed	Processed
1	Common phenolic compounds - %	5.2	6.9
2	Oligomeric proanthocyanidins - %	0.7	0.9
3	Polymeric proanthocyanidins - %	4.5	6.0
4	Catechins - %	0.5	0.7
5	Flavonols - %	0.11	0.15
6	Common coloring substances - %	3.2	4.5

The sugar concentration in the juice of Chkhaveri grapes grown on soil not treated with a biostimulant was 18%, and in soil treated with a biostimulant, it was 20%. The variation in the total concentrations of compounds representing bioflavonoids was observed to be of different magnitudes. The results obtained convinced us to continue research in this direction. Therefore, in 2024, we increased the options for biostimulant treatment and, accordingly, the objects of research. We are conducting research to determine the variability of biologically active flavonoids and non-flavonoid phenolic compounds in Chkhaveri grapes in relation to the biostimulant.

References

1. Prieur C., Rigaud J., Cheynier V., Moutounet M. Oligomeric and polymeric procyanidins from grape seeds // Phytochemistry, 1994, V. 26. P. 781-784.

2. Ribereau-Gayon P. Les flavonoids de la baie dans le genre Vitis // Compt. Rend. Acad. Sci. France, 1964, N. 258. P. 1335-1337.

3. Ribereau-Gayon P. Localization of procyanidins in grape seeds // Am. J. Enol. Vitic. 1994, V. 45. P. 259-262.

4. Shalashvili A., Ugrekhelidze D., Targamadze I., Zambakhidze N., TsereteliL. Phenolic Compounds and Antiradical Efficiency of Georgian (Kakhetian) Wines. Journal of Food Science and Engineering, 2011 n.1. pp. 1-5.

5. Положникова М.А., Перелыгин О.Н. Determination of biological value and identification of red grape wines by the content of flavonoids and phenolic acids . // Виноделие и вногодарство , 2005 , №6 с . 22 24 .

6. Puértolas E. , Alvarez I. , Raso J. Changes in phenolic compounds of Aragon red wines during alcoholic fermentation. Tecnología de los Alimentos, Facultad de Veterinaria, Universidad de Zaragoza, Spain. Food Sci Technol Int. 2011 Apr;17(2):77-86.

7. Durmishidze S. , Khachidze O. Biochemistry of the Vine . 1985.561 p .

8. Beecher GR Overview of Dietary Flavonoids: Nomenclature, Occurrence and Intake // J. Nutr. - 2003. - Vol. 133, No. 10. – P. 3248-3254.

9. Goodwin T., Mercer E. Plant phenols // Introduction to biochemistry of plants. - Moscow, 1986. - Гл. 14. – С. 167-202.

10. Barz W., Harborne JB, Mabry T. J., Mabry. H. The Flavonoids. - New York: Acad. Press, 1975. - 1204 p.

11. Navarre K. , Langlade F. Enology , Lavoisier 2004 (first Georgian edition , G. Samanishvili), 361 p .

12. Brown JE , AndersenM. K. , MarkhamR. Flavonoids: chemistry, biochemistry, and applications - Boca Ratton: CRC Press, 2006. -1197 p.

13. Kishkovsky Z.N., Skurihin I.M. Chemistry is the fault. M. Пишчепромизд. 1976. 311 st.

14. Durmishidze C.B. Г allokatechin in the composition of tanning substances. Doc. AN SSSR, 77, 5ю 1951. c. 859-862.

15. Durmishidze C.B., Nutsubidze H.H. Chromatographic studies of tannins of grape vine. Doc. AN USSR, 1954 . c. 1197-1199.

16. DurmishidzeC . B. Tanning substances and anthocyanins of grape vines . 1955 , M .: Изд - воАНСССР . 323 с .

17. DurmishidzeC . B ., NutsubidzeH . N. Anthocyanin pigments of grapes . СообщенияАНГССР . 1958 . т . 21 , No. 6 , с . 677 - 684 .

18. Ribereau - Gayon P. Lescomposes phenolquesderaisinetduvin . Ann . Phusiol . vegetables . 1964 , 6 , N2 . p . 119 - 139 .

19. Марх А.Т., Зыкина Т.Ф. Chromatographic study of polyphenols in grapes and grape juice. Прикл. Biokh. и микробиол., 5, 2, 1969. с. 189-194.

20. Durmishidze S. Khachidze Oh . Chemical composition of grapes . " Science " Tbilisi , 1979 . 191 pages ;

21. Durmishidze S. , Khachidze . Vine Biochemistry . Tbilisi , Publishing House , 1969. 354 pages .

22. Gelashvili N.N., Jemukhadze K.M. Состав catechins of grapes Ркацители. Сообщения АН ГССР, т. 58, No. 1, 1970. p. 22-23.

23. Nutsubidze H.H. Превращение катехинов в процессие технологии вин типа Мадера. Autoref. dissertation. работы, представленной на соискании учечной страница кандида биологических наук. Tbilisi, 1956. 17 с .

24. Valuyko G. G. Biochemistry and technology of red wines. Food industry. M. 1973 - 295 c.

25. Риберо-Гайон Ж., Пейно Э., Риберо-Гайон П., Сюдро П. Theory and practice of winemaking. T. 3. 1980.79 с .

26. Singleton VL, Esau P. Phenolic substances in grapes and wine and their significance. Acad. Press, New-York-London. 1969.

27. Shalashvili* A. , Ugrekhelidze** D., Mitaishvili* T., Targamadze* I., Zambakhidze* N. Phenolic compounds of wines made according to the Georgian (Kakhetian) method from the autochthonous grape varieties of Georgia: Rkatsiteli and Saperavi. Bull. Georg. Natl. Acad. Sci., vol. 6, no. 3, p. 2012.

28. Edelmann A., Diewok J., Schuster K.C., Lendl. B., Rapid method for the discrimination of red wine cultivars based on mid-infrared spectroscopy of phenolic wine extracts // J. Agric. Food Chem. 2001, V. 49. N. 3. P. 1139-1145.

29. McDonald MS, Hughes M., Burns J. Survey of the free and conjugated myricetin and quercetin content of red wines of different geographical origins // J. Agric. Food Chem. 1998, V. 46. P. 368-375.

30. Valuyko Г.Г. Biochemistry and technology of red wine. M., Пищеваяпромышленность, 1973, 256 с.

31. Brown JE, Andersen M., Markham KR Flavonoids: chemistry, biochemistry, and applications / - Boca Ratton: CRC Press, 2006. -1197 p.

32. Nutsuvidze N.N., Gulbani D.I.//Сообщения АН ГССР, т.XX, XVI, №2, 1964, с. 345-347.

33. Sun Y., Liang F., Bin Y., Li P. and Dian Ch. Screening Non-colored Phenolics in Red Wines using Liquid chromatography/Ultraviolet and Mass Spectrometry/Mass Spectrometry Libraries. //Molecules, 2007, vol. 12, pp. 679-693.

34. Yustesen U., Knuthsen P. The use of HPLC and mass spectrometry for the determination of flavonoids in red wines. 2nd International Electronic Conference on Synthetic Organic Chemistry · 1998, 1-30 September.

35. Bezhuashvili M. Г., МесхиM. Yu., Bostoganashvili M. V., Malania M. A. Phenolic sources and Antioxidative Activity vinomaterialov, intended for for wine Catechin Type. «Виноделиеи Виноградарство». 2005. No. 5. С. 28-29.

36. GrozierA. , BurnsY., AzizA., StewartA., RabiaszH., YenkinsG., EdwardsCh. andLeanM. Antioxidantflavonls from fruits, vegetables and beverages: measurements and bioavailability. //Biological research. Santiago, 2000, vol. 33, N2.

37. Daniel O., Samuel Meier M., Schatter Y. and Frischknecht P. Selected Phenolic Compounds in Cultivated Plants: Ecological Functions, Health Implications and Modulation by Pesticides. //Environ Health Perspective. 1999, vol. 107, N51, pp. 109-114.

38. Bokuchava M. A ., Valuiko Г . Г ., Ulyanova M . С ., Стурya З . M. Determination of flavonols of grapes and wines by thin - layer chromatography on cellulose . 1971 .- Vyl . 4.- С. 503 505 .

39. Стурya З. Sh., Bokuchava M.A., Valuyko G.G., Erofeeva N.N., Siashvili A.I. Applied Biochemistry and Microbiology, 7, No. 5, 1971. 606-608.

40. Rodopulo A. K. Biochemistry of winemaking. 1971, М.: Пищеваяпромышленность, с. 372 .

41. Yustesen U., Knuthsen P. The use of HPLC and mass spectrometry for the determination of flavonoids in red wines. 2nd International Electronic Conference on Synthetic Organic Chemistry · 1998, 1-30 September.

42. Shonia T. Bezhuashvili M. Pataraya M. Dynamics of accumulation of total flavonols in wine materials of Kakhetian and Imeretian types. //Magarach. Winemaking and winemaking. 2006. No. 4. — 19-20 с.

43. BezhuashviliM.Г., ШонияТ.М. Влияние винных дрожжей на превращения на превращения земый flavonolos выногра при алконовном брожении.//Виноделие и вногодарство. 2008. No. 5, p. 22-24.

44. Shonia T. M., Bezhuashvili M. G., Aplakov V. R. Influence of some wine yeasts on the conversion of dihydroflower in alcoholic fermentation. GeorgianEngineeringNews . 2009. N 1. P. 193-195.

45. Alexandros D., Tselepis A., Evangelia S., Lourida A., Panagiotis C., Tzimas B., Ioannis G. Comparative Antioxidant Effectiveness of White and Red Wine and Their Phenolic Extracts Towards Low-Density Lipoprotein Oxidation . // Ioannina, Greece.// Food Biotechnology, Volume 19 , 2005, p . 1 - 14 .

46. Nutsubidze N. N., Gulbani D. И. Сообщ. AN ГрузССР, 1959, 23, 6.

47. Kvlividze D. , Bezhuashvili M. Agricultural and technological features of Saperavi in the Khashmi microzone . // “ Moambe ” of the Georgian Academy of Agricultural Sciences . 2005. Vol.14, pp. 47-55.

48. Weinges K., Piretti MV Isolation of procyanidin B1 from grapes//Justus Liebigs Ann. Chem. 1971, V. 748. P. 218-220.

49. Powell HKJ, Rate AW Aluminum-tannin equilibria: a potentiometric study // Aust. J. Chem. 1987. Vol. 40.P. 2015–2022.

50. Santos-Buelga C., Scalbert A. Proanthocyanidins and tannin-like compounds – nature, occurrence, dietary intake and effects on nutrition and health // J. Sci. Food Agric. 2000. Vol. 80, N 7. P. 1094–1117.

51. Vephishvili N. G., Vezhuashvili M.G., Javakhishvili M.L. Sortrvye features according to the phenolic spectrum in Georgian red wines. GeorgianEngineeringNews , 2010 . #3, pp . 99-102 .
52. Bezhuashvili M.G., Deisadze I.M. , Kobaidze T.A. Correlation of proanthocyanidins and purity in red wine materials from Technical varieties and hybrids - direct producers. ВиноделиеиВиноградарство . 2008 . No. 3. c .20-22.

53. SunB. S. , Pinto T. , Leandro MC , Ricardo-Da-SilvaJ. M. , Spranger MI Transfer of Catechins and Proanthocyanidins From Solid Parts of the Grape Cluster Into Wine. American Journal of Enology and Viticulture. by BS Sun - 1999 - Cited by 92 .

54. Hanlin R. L, Kelm M. A, Wilkinson K. L, Downey M. O. Detailed characterization of proanthocyanidins in skin, seeds, and wine of Shiraz and Cabernet Sauvignon wine grapes (Vitis vinifera). J Agric Food Chem. 2011 . Dec 28;59(24):13265-76.

55. Sanchez -Moreno C. , Cao G. , Ou B. , Prior R. L. Anthocyanin and proanthocyanidin content in selected white and red wines. Oxygen radical absorbance capacity comparison with non-traditional wines obtained from highbush blueberry. J Agric Food Chem 51: 2003 . P. 4889–4896.

56. Monagas M. , Suarez R. , Gomes - Cordoves C. , Bartolome B. Simultaneous Determination of Nonanthocyanin Phenolic Compounds in Red Wines by HPLC - DHD/ESI - MS . Am . j . Enol . Vitic . 2005 , vol . 56 . N2 , p . 139 - 147 .

57. Valuyko G. G. Biochemistry and technology of red wine. M., Пишчевая промышленность, 1973, 256 c.

58. Su T. C., Singleton, V. L. Identification of three flavan-3-ols from grapes // Phytochemistry. 1969, V. 8. P. 1553-1558.

59. Weinges K., Piretti MV Isolation of procyanidin B1 from grapes//Justus Liebigs Ann. Chem. 1971, V. 748. P. 218-220.

60. BenthsathA. / Vitamin nature of flavones / / Nature. - 1936. - Vol. 138. – P. 798.

61. Middleton E. The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease, and cancer. Jr. Pharmacol. Rev. - 2000. - Vol. 52, No. 4. – P. 673-751.

62. Willcox JK Antioxidants and prevention of chronic diseases. // Crit. Rev. Food Sci. Nutr. - 2004. - Vol. 44, No. 4. – P. 275-295.

63. Soobrattee MA Phenolics as potential antioxidant therapeutic agents: Mechanism and actions // Mutat. Res. - 2005. - Vol. 579, No. 1/2. - P. 200-213.

64. Stevenson, DE Polyphenolic phytochemicals – just antioxidants or much more. / Hurst // Cell. Mol. Life Sci. - 2007. - Vol. 64, No. 22. – P. 2900-2916.

65. Havinson V. X. Free radical oxidation and aging . - St. Petersburg: Наука, 2003. - 327 с.

66. Singh M. Challenges for research on polyphenols from foods in Alzheimer's disease: Bioavailability, metabolism, and cellular and molecular mechanisms. // J. Agric. Food Chem. - 2008. - Vol. 56, No. 13. – P. 4855–4873.

67. Kostyuk V. A. , Потапович А. И. Биорадикалы и биоантиоксидант - Минск: БГУ, 2004. - 179 с.

68. Seyoum A. Structure-radical scavenging activity relationships of flavonoids . // Phytochemistry. - 2006. - Vol. 67, No. 18. – P. 2058-2070.

69. Kandaswami C., E. Middleton. Free radical scavenging and antioxidant activity of plant flavonoids. / Jr. // Adv. Exp. Med. Biol. - 1994. - Vol. 366. - P. 351-376.

70. Wright JS Predicting the activity of phenolic antioxidants: theoretical method, analysis of substituent effects, and application to major families of antioxidants // J. Am. Chem. Soc. - 2001. - Vol. 123, No. 6. – P. 1173-1183.

71. Jovanovic SV Flavonoids as antioxidants. // J. Am. Chem. Soc. - 1994. - Vol. 116, No. 11. – P. 4846-4851.

72. Fiorucci S. DFT study of quercetin activated forms involved in antiradical, antioxidant, and prooxidant biological processes // J. Agric. Food Chem. - 2007. - Vol. 55, No. 3. - P. 903-911.

73. Kostyuk, VA, Potapovich AI Superoxide--driven oxidation of quercetin and a simple sensitive assay for determination of superoxide dismutase.// Biochem. Int. - 1989. - Vol. 19, No. 5. – P. 1117-1124.

74. Wilms LC Discriminative protection against hydroxyl and superoxide anion radicals by quercetin in human leucocytes in vitro. // Toxicol. In Vitro. - 2008. - Vol. 22, No. 2. – P. 301-307.

75. Papa S., Skulachev VP Reactive oxygen species, mitochondria, apoptosis and aging /. // Mol. Cell Biochem. - 1997. - Vol. 174, No. 1/2. - P. 305-319.

76. Pourcel L. Flavonoid oxidation in plants: from biochemical properties to physiological functions. // Trends Plant. Sci. - 2007. - Vol. 12, No. 1. – P. 29-36.

77. Egley GH Peroxidase involvement in lignification in water-impermeable seed coats of weedy leguminous and malvaceous species. // Plant, Cell & Environ. - 1985. - Vol. 8, No. 4. - P. 253-260.

78. Bailly C. Active oxygen species and antioxidants in seed biology / C. Bailly // Seed Sci. Res. - 2004. - Vol. 14, No. 2. – P. 93-107.

79. Aziz NH Comparative antibacterial and antifungal effects of some phenolic compounds.// Microbios. - 1998. - Vol. 93, No. 374. - P. 43-54.

80. Walker JR, Ferrar PH Diphenol oxidases, enzyme-catalyzed browning and plant disease resistance. // Biotechnol. Genet. Eng. Rev. - 1998. - Vol. 15. – P. 457-498.

81. Rahman M., Punja ZK Biochemistry of ginseng root tissues affected by rusty root symptoms. // Plant Physiol. Biochem. - 2005. - Vol. 43, No. 12. – P. 1103-1114.

82. Feeny PP Plant appearance and chemical defense. // Rec. Adv. Phytochem. - 1974. - Vol. 10. – P. 1-40.

83. Walle T. Absorption and metabolism of flavonoids. // Free Radical. Biol. Med. - 2004. - Vol. 36, No. 7. – P. 829-837.

84. Clemetson CA, Andersen L. Plant polyphenols as antioxidants for ascorbic acid. // Ann. NY Acad. Sci. - 1966. - Vol. 136, No. 14. - P. 341-376.

85. Korkina LG Metabolism of plant polyphenols in the skin: beneficial versus deleterious effects. // Curr. Drug Metab. - 2008. - Vol. 9, No. 8. - P. 710-29.

86. Stavric B. Quercetin in our diet From potent mutagen to probable anticarcinogen. //Clinical Biochemistry. 1994, N27, pp. 245-248.

87. Vrijsen R., Everaert L., and Boeje A. Antiviral activity of flavones and potentiation by ascorbate. //Journal of Genealogy and Virology. 1998. vol. 69, pp. 1749-1751.

88. Bezhuashvili M.Г., Meskhi M.Ю., Bostoganashvili M.B., Малания M.A. Antioxidative activity of stilbene-containing extract in in vitro experiments . Winemaking and winemaking. 2005. No. 3. p. 26-27.

89. Conquer YA, Maiani G., Azzini E., Raguzzini A. and Hobub BY Supplementation with quercetin markedly increases plasma quercetin concentration without effect on selected risk factors for heart disease in healthy subjects. //Jpurnal of Nutrition. 1998, vol. 128, pp. 595-597.

90. Takahama U. Inhibition of lipoxygenase-dependent lipid peroxidation by quercetin: Mechanism of antioxidative function. //Phytochemistry. 1985, vol. 24. pp. 1443-1446.

91. Pace-Asciak CR, Haln S., Diamandis EP, Soleas G. and Goldberg DM The red wine phenolics trans-resveratrol and quercetin block human platelet aggregation and eicosanoid synthesis: Implications for protection against coronary heart disease. //Clinica Chemista Acta. 1995. vol. 235. pp. 207-219.

92. De Beer, D., Joubert E., Gelderblom WCA, Manley M. Antioxidant activity of South African red and white cultivar wines: Free radical scavenging. J. Agric. Food Chem. 2003, 51, 902-909.

93. Zafrilla P , Morillas J , Mulero J , Cayuela JM , Martínez-Cachá A , Pardo F , López Nicolás JM . Changes during storage in conventional and ecological wine: phenolic content and antioxidant activity. / J Agric Food Chem. 2003 Jul 30;51(16):4694-700 .

94. Campos AM, Lissi EA Total antioxidant potential of Chilean wines. Nutr. Res. 1996, 16, 385-389.

95. Simonetti P., Pietta P., Testolin G. Polyphenol content and total antioxidant potential of selected Italian wines. J. Agric. Food Chem. 1997, 45, 1152-1155.

96. Landrault N., Poucheret P., Ravel P., Gasc F., Cros G., Teissedre PL. Antioxidant capacities and phenolics levels of French wines from different varieties and vintages. J. Agric. Food Chem. 2001, 49, 3341-3348.

97. De Beer D., Joubert E., Gelderblom WCA, Manley M. Antioxidant activity of South African red and white cultivar wines and selected phenolic compounds: In vitro inhibition of microsomal lipid peroxidation. Food Chem. 2005, 90, 869-577.

98. Bertelli AF, Giovenni L., Gianessi D., Miglior M., Bernini W., Fregoni M., Bertelli A. Antiplatelet activity of synthetic and natural resveratrol in red wine. Int. J. Tissue React. 1995, 17 .- pp. 1-3 .

99. Bezhuashvili M. G., Chkhartishvili E. P., Bostoganashvili M. B., Малания М. А. Antioxidative activity of anthocyanins of wine material «Саперави»: Влияние pH на неё в опытах invitro . Winemaking and winemaking. No. 4, (2005) с. 20-21.

100. Weisse ME, Eberlg B., Person B. Wine as a Digestive Aid: comparative antimicrobial effects of biosmuth saliculate and red and white wine. BMY. 1995, 311, pp. 1657-1660 .

101. KlatskyA. , ArmstrongM. , FriedmanG. Red wine, white wine, liquor, beer and risk for coronary artery disease hospitalization. American Journal of Cardiology 80(1997) 416-420.

102. Constant J. Alcohol, ischemic heart disease and French paradox. Clinical Cardiology. 1997, 20, pp. 420-424 .

103. Jarret.N., Peatfield R., Glover V. Red wine is less stress reducing than vodka; no differences in neuroendocrine, challenge test. Journal of Psychopharmacology. 1997, 11, pp. 283-286 .

104. Grande l., Manterola C., Roc E. Lacima G., Pera C. Effect of red wine on 24-hour esophageal pH and pressures in healthy volunteers. Digestive Diseases and Sciences. 1997, 42, pp. 1189-1193.

105. Viel JF, Perarnou JM, Challier B., Fairve-Nappes I. Alcoholic calories, red wine consumption and breast cancer among premenopausal women. European Journal of epidemiology. 1997. 13. Pp. 639-643 .

106. Lugasi A., Blazovics A., Dworschk E., Fehel Y. Cardio-protective effect of red wine as reflected in the literature. Orvosi Hetilap. 1997.138, pp. 673-678 .

107. Kondo K., Matsumoto A., Kurata H., Tanahashi H., Koda H., AmachiT., Itakura H. Inhibition of oxidation of low-density lipoprotein with red wine. Lancet. 344(1994) 115-119 .

108. De Rijke YB, Demacker PN Assen M. Et al. Red wine consumption and oxidation of low-density lipoproteins. Lancet. 1995, 345, pp. 325-326 .

109. Frankel EN, Kanner YB, Parks E., Kinsella YE Inhibition of oxidation of human Low-Density Lipoprotein by phenolic substances in red wine. Lancet. 1993, 341, pp. 454-457 .

110. Abu-Amsha-Caccetta R. Red wine polyphenols, in the absence of alcohol, reduce lipid peroxidative stress in smoking subjects. Free-Radic-Biol-Med. 2001. 30(6): 636-42;

111. CaccettaR . A. Ingestion of red wine significantly increases plasma phenolic acid concentrations but does not acutely affect ex vivo lipoprotein oxidizability. Am-J-Clin-Nutr. 71(1): 67-74; 2000.

112. Маслова **Л.Н.** About the prospects of using flavonoids for the prevention of atherosclerosis and atherothrombosis. Издание: Клиническая фармако логиаитерапия . 2007.- N 3.-С.60-67.

113. Chan MMY. Antimicrobial effect of resveratrol on dermatophytes and bacterial pathogens of the skin. Biochemical Pharmacology .2002; 63: 99-104.

114. Daroch F [1] ., Hoeneisen M ., González CL ., Kawaguchi F ., Salgado F ., Solar H ., García A . In vitro antibacterial activity of Chilean red wines against Helicobacter pylori. Microbios. 2001;104(408):79-85.

115. Feringa HHH, Laskey DA, Dickson JE, Coleman CI "The effect of grape seed extract on cardiovascular risk markers: a meta-analysis of randomized controlled trials," Journal of the American Dietetic Association, vol. 111, no. 8,. pp. 1173–1181. 2011.

116. Mellen PB, Daniel KR, Brosnihan KB, Hansen KJ, Herrington D. M. "Effect of muscadine grape seed supplementation on vascular function in subjects with or at risk for cardiovascular disease: a randomized crossover trial," Journal of the American College of Nutrition, vol. 29, no. 5, pp. 469–475, 2010 .

117. Kar P. , Laight DH, Rooprai K., Shaw KM, Cummings M. "Effects of grape seed extract in Type 2 diabetic subjects at high cardiovascular risk: a double blind randomized placebo controlled trial examining metabolic markers, vascular tone, inflammation, oxidative stress and insulin sensitivity". Diabetic Medicine, vol. 26, no. 5, pp. 526–531, 2009.

118. Castilla P., Dávalos A., Teruel JL "Comparative effects of dietary supplementation with red grape juice and vitamin E on production of superoxide by circulating neutrophil NADPH oxidase in hemodialysis patients," American Journal of Clinical Nutrition, vol. 87, no. 4, pp. 1053–1061, 2008 .

119. Castilla P., Echarri R., Dávalos A. "Concentrated red grape juice exerts antioxidant, hypolipidemic, and anti-inflammatory effects in both hemodialysis patients and healthy subjects," American Journal of Clinical Nutrition, vol. 84, no. 1, pp. 252–262, 2006.

120. Brooker S., Martin S., Pearson A. "Double-blind, placebo-controlled, randomized phase II trial of IH636 grape seed proanthocyanidin extract (GSPE) in patients with radiation-induced breast induration," Radiotherapy and Oncology, vol. 79, no. 1, pp. 45–51, 2006.

121. Preuss HG, Wallerstedt D., Talpur N. "Effects of niacin-bound chromium and grape seed proanthocyanidin extract on the lipid profile of hypercholesterolemic subjects: a pilot study," Journal of Medicine, vol. 31, no. 5-6, pp. 227–246, 200 0 .

122. BASTIANETTO S., ZHENG WH, QUIRION R. Neuroprotective abilities of resveratrol and other red wine constituents against nitric oxide-related toxicity in cultured hippocampal neurons. Bro. J. Pharmacol. 2000;131:711–720.

123. JIANG F., DUSTING GJ Natural phenolic compounds as cardiovascular therapeutics: potential role of their anti-inflammatory effects. Curr. Vasc. Pharmacol. 2003;1:135–156.

124. MANDEL S., WEINREB O., YOUDIM MBH Using cDNA microassay to assess Parkinson's disease models and the effect of neuroprotective drugs. Trends Pharmacol. Sci. 2003;24:184–191.

125. Romero I., Paez A., Ferruelo A., lujan M. Berenguer A. Polyphenols in red wine inhibit the proliferation and induce apoptosis of LNCaP cells, BJUInternational , 89: 950-954, 2002.

126. Локатская Л. Bioflavonoids: known properties, new opportunities // Les news aesthetics . - 2007. No. 6. - c . 144-149.

127. Yao, LH; Jiang, YM; Shi, J.; Tomás-Barberán, FA; Datta, N.; Singanusong, R.; Chen, SS Flavonoids in food and their health benefits. Plant Foods Human Nutr. 2004 , *59* , p.113-122.

128. Ferguson, PJ; Kurowska, E.; Freeman, DJ; Chambers, AF; Koropatnick, DJ A flavonoid fraction from cranberry extract inhibits proliferation of human tumor cell lines. J. Nutr. 2004 , 134, p.1529-1535.

129. Havsteen, B. Flavonoids, a class of natural products of high pharmacological potency. Biochem. Pharm. 1983 , 32, p. 1141-1148.

130. Lyons-Wall, PM; Samman, S. Flavonoids - dietary perspectives and health benefits. Nutr. Soc. Aust. 1997 , 21, p. 106-114.

131. Ma, TE; Celestino, S.; Julián, CR Anthocyanins in cereals. J. Chromatogr. A 2004 , 1054, p.129-141.

132. Moon, YJ; Wang, XD; Morris, ME Dietary flavonoids: Effects on xenobiotic and carcinogen metabolism. Toxicol. Vitro 2006 , 20 , pp.187-210.

133. Duan, XW; Jiang, YM; Su, XG; Zhang, ZQ; Shi, J. Antioxidant properties of anthocyanins extracted from litchi (Litchi chinenesis Sonn.) fruit pericarp tissues in relation to their role in the pericarp browning. Food Chem. 2007 , 101, p.1382-1388.

134. Edelmann A., Diewok J., Schuster K. C. , Lendl. B., Rapid method for the discrimination of red wine cultivars based on mid-infrared spectroscopy of phenolic wine extracts // J. Agric. Food Chem. 2001, V. 49. N. 3. P. 1139-1145.

135. Cossins E., Lee R., Packer L., ESR studies of vitamin C regeneration, order of reactivity of natural source phytochemical preparations. Biochem // Mol. Biol. Int. 1998, V. 45. N. 3. P. 583-597.

136. Hertog MGL Les flavonoides dans le, le vin rouge et les ignons protegnet - ils contre les maladies cardio vasculaires et le cancer? // Polyphenols Actualites.- 1995 - No. 13. -pp. 17-19.

137. Day AJ, Bao Y., A Morgan MR, Williamson G. Conjugation position of guercetin glucoronides and effect on biological activity. Volume 29, Issue 12, 15 December 2000, P.1234-1243.