Review Paper

Can fruit wines be considered as functional food? —An overview

Gargi Dey*, **Bharti Negi and Akanksha Gandhi**
Department of Biotechnology & Bioinformatics
Jaypee University of Information Technology
Waknaghat, Solan-173 215, Himachal Pradesh, India
*Correspondent author, E-mail: gargi.dey@juit.ac.in, drgargi.dey@gmail.com

Received 12 April 2009; Accepted 11 June 2009

Abstract

We are in midst of antioxidant superfood revolution. Nutritional studies on examining the foods for their protective and disease preventing potential have established that apart from grapes, fruits like cranberry, sweet cherry, blue berry are equal or sometimes better sources of flavonoids and phenolics. These facts have given a new dimension to the non-grape wines or fruit wines. A lot of efforts have been directed towards potential use of these fruits for production of wines which are rich in phenolics and flavonoids. This paper presents an overview on the phenolic and flavonoid contents of the non-grape wines or fruit wines and their antioxidant potency. It has also been tried to answer the question, whether fruit wines can also be considered as functional food.

Keywords: Fruit wines, Phenolics, Flavonoid, Antioxidant activity, Berry wines, Functional food.

IPC code; Int. cl.[8]—C12G 1/00, A61P 17/18

Introduction

Cultural beliefs in the mystical powers of foods have been handed down for generations. The ability of specific foods to prevent or reduce the severity of symptoms arising from what are now frequently recognized as nutritional inadequacies has been recorded in a variety of historical documents[1]. This widespread interest in the possibility that selected foods might promote health has resulted in the coining of the term Functional Food. This term was first introduced in Japan in the mid 1980 and refers to processed foods containing ingredients that aid specific bodily functions in addition to being nutritious. To date, Japan is the only country that has formulated a specific regulatory approval process for functional foods, known as Foods for Specified Health Use (FOSHU).

The concept of functional food, though not new, has evolved considerably over the years. They can include whole foods as well as fortified, enriched or enhanced foods and dietary supplements that have beneficial effect on health. Thus, functional food cannot be a single well-defined entity. Controversies about what is and what is not a functional food remain at the forefront of discussions[2-4]. The Food and Nutrition Board (FNB) of the National Academy of Sciences defines a Functional Food as one that encompasses potentially healthful products, including "any modified food or food ingredient that may provide a health benefit beyond that of the traditional nutrients it contains"[5]. In the broadest context, all foods must be considered "functional". Nevertheless, some foods may be particularly beneficial in selectively altering specific physiologic processes that improve the quality of life or reduce the risk of acquiring a disease. Hence, it might be safe to say that foods which have now assumed the status of functional food should be capable of providing additional physiological benefit, such as preventing or delaying onset of chronic diseases, as well as meeting basic nutritional requirements.

New functional food ingredients are being discovered every day and consumer demand for "food with a healthy function" is a growing trend. We seem to be in the midst of an antioxidant superfood revolution and functional foods infused with antioxidants, omega fatty acids, fibres and/or protein enriched whole grain foods and nutrient fortified beverages are becoming a common feature. The high content of secondary metabolites present in fruits including phenolics, vitamins and minerals which give them both nutritional and therapeutic quality and have brought the focus back on fruits and vegetables. Processed products of various fruits such as juices do contain these nutraceutical compounds. With respect to wine, after the phenomenon called "French paradox" lot of research has been focused on the phenolic compounds of red wine[6]. At present it is a well established fact that the red wine gets its antioxidant and anti-inflammatory properties due to the phenolic constituents[7-9]. Wine phenolics have also been reported to induce endothelial nitric oxide dependent vasorelaxation to inhibit oxidation of human low density lipoproteins and platelet-aggregation[10-13]. Like wise the anticarcinogenic activity of wine phenolics have also been demonstrated[14]. From all these reports one things is well established that the phenolics and flavonoids of red wine have therapeutic potential. This fact has spurred the researchers to explore the potential use of other fruits, with higher phenolic content compared to grapes, for the production of nutraceutical wines.

In past, fruits other than grapes i.e., plum, peach, apples, apricots, etc. have been utilized for production of wines. The production methodology and the characteristic properties of different types of fruit wines have been extensively reviewed by Joshi *et al*[15]. However, for some reason, the amount of fruit wines have been less as compared to grape wines produced and consumed. Nutritional studies concentrating on examining foods for their protective and disease preventing potential have established that fruits apart from grapes like cranberry, sweet cherry and blue berry are equal or sometimes better sources of flavonoids and phenolics. In fact, berries are not only delicious but also low energy food and a rich source of antioxidant, vitamins, fibre and various phenolics compounds. Cranberry juice has been recognized for a long time to be effective in the treatment of urinary tract infections (UTI) and oxidative effects[16]. Proanthocyanidins or condensed tannins present in blue berries have been identified as compounds responsible for preventing UTI caused by *Escherichia coli*. Earlier studies have also shown that many berries are rich in flavonols[17-20]. The total content of the flavonols quercetin, myricetin and kaempferol is higher in cranberry, bog whortle berry, lingonberry, crowberry and black currant than in the commonly consumed fruits or vegetables, with the exceptions of onion and kale. A detailed study on the berry phenolic contents further confirmed the above facts[20, 21]. It was reported that in ***Vaccinium*** sp. that is, bilberry, bog-whortleberry and cranberry, anthocyanins were the major phenolic subgroup except in cowberries, in which the flavanol and procyanidin concentration exceeded the anthocyanin concentration. In family Rosaceae, genus ***Rubus*** **Linn.** (Cloudberry and Red raspberry) and in genus ***Fragaria*** **Linn.** (Strawberry), ellagitannins predominated. Rowan and chokeberry are members of the same Rosaceae family, but ellagitannins were detected in neither one of them; hydroxycinnamates were dominant in rowanberries (genus ***Sorbus*** **Linn.**) and anthocyanins in chokeberry (genus ***Aronia***). In black and red currants and gooseberry, belonging to family Grossulariaceae genus ***Ribes*** **Linn.**, anthocyanins predominated, as well as in crowberries (family Empetraceae genus ***Empetrum***). In apples, the phenolic content was fairly low, hydroxycinnamates being the main phenolic subgroup[21].

The most compelling evidence of superior nutraceutical values of berries comes from the recent USDA Database for the Oxygen Radical Absorbance Capacity (ORAC) of selected Foods[22]. ORAC values are reported for hydrophilic-ORAC (H-ORAC), lipophilic-ORAC (L-ORAC), total-ORAC and total phenolics (TP). H-ORAC, L-ORAC and total-ORAC are reported in μmol of Trolox Equivalents per 100g (μmol TE/100g), while TP is reported in mg gallic acid equivalents per 100g (mg GAE/100g). ORAC values of some of the fruits have been compiled in Table 1 which clearly shows that compared to red grapes, fruits like black and blue berries, choke berries, cranberries, sweet cherries, black and red currants, elderberries, raspberries and strawberries show much higher ORAC activity and total phenolics. The antioxidant activity of berries and the presence of wide range of flavonoids have made berries an important source of non-grape wines. This has led to researchers turning their focus on study of berry and other fruit wines.

In order to answer the question whether fruit wines can be considered "functional" or not one has to examine whether there are enough nutraceutical compounds in the fruit wines. In the present paper literature on some of the fruit wines, considered as functional food (on the basis of their total phenolics, flavonoids, antioxidant activity and elemental composition) has been reviewed.

Total phenolics

Phenolic substances in wine include both non-flavonoids such as hydroxybenzoates and hydroxycinnamates and stilbene along with flavonoids such as flavonols, anthocyanins and polyphenol tannins. The phenolic components are inhibitors of *in vitro* oxidation of low density lipoproteins[23]. Flavonoids may provide protection against these diseases by contributing, along with antioxidant vitamins and enzymes, to the total antioxidant defence system of the human body. Epidemiological studies have shown that flavonoid intake is inversely related to mortality from coronary heart disease and to the incidence of heart attacks. Clearly the nutraceutical potential of wines is due to the phenolic and flavonoid components.

So far, the detailed study reported on fruit wine phenolics and antioxidant activity is by Heinonen *et al*[24]. A total of 44 different berries and fruit wines and liquors were evaluated for antioxidant activity. The amount of total phenolics in the berry and fruit wines and liquors ranged from 91 to 1820 mg GAE/l. Wines made of cherries (1080 mg GAE/l), red raspberries and black currants (1050 mg GAE/l), black currants and bilberries (average 1040 mg GAE/l), black currants and crowberries (1020 mg GAE/l), black and red currants (average 890 mg GAE/l) and black currants (average 870 mg GAE/l) contained the highest amounts of phenolic compounds. Marked amounts of total phenolics were also present in wines made of crowberries and birch sap (776mg GAE/l) as well as in wines made of mixtures of black and/or red currants and strawberry (average 755mg GAE/l). Later in 2006, Yildirim[25] had evaluated the total phenolic content of fruit wines and arranged in the following order blackberry>bilberry>black mulberry>sour cherry>strawberry> raspberry>quince>apple> melon>apricot.

Recently total phenolics from different fruit wines were also estimated where wines from elderberry and blue berry were found to have 1753 and 1676 mg GAE/l, respectively[26]. Figure 1 shows the compilation of total phenolic values of fruit wines collected from different studies and clearly the fact that emerges is wines from black currant, black and red currant, blue berry and elderberry seem better than grape wines like Cabernet and Merlot[26, 27]. Other wines from raspberry, cherry, black currant and bilberry, black currant and raspberry were also comparable to those of red wines. However, other fruit wines like apple, plum and peach showed lower levels of phenolics. Fruits like Seabuckthorn (***Hippophae rhamnoides*** **Linn.**) have been reported to be a gold mine of nutraceutical compounds[28]. A study reported that total flavones of ***H. rhamnoides*** had an effect similar to that of aspirin on *in vivo* thrombogenesis and it has been reported that aspirin prevents secondary events in cardiac and cerebral disease[29, 30]. Based on these findings, an attempt has been made in our lab to convert the commercial Seabuckthorn juice (Leh Berry) into wine using lab isolated yeast strain and the total phenolic content of the wine was estimated as 689 mg GAE/l. Other wines made in our lab, with the same lab strain were found to have a total phenolic content in the following order: sea buckthorn (689 mg GAE/l) > grape wine (647 mg GAE/l) > black currant wine (323 mg GAE/l) > apple wine (177 mg GAE/l)[31].

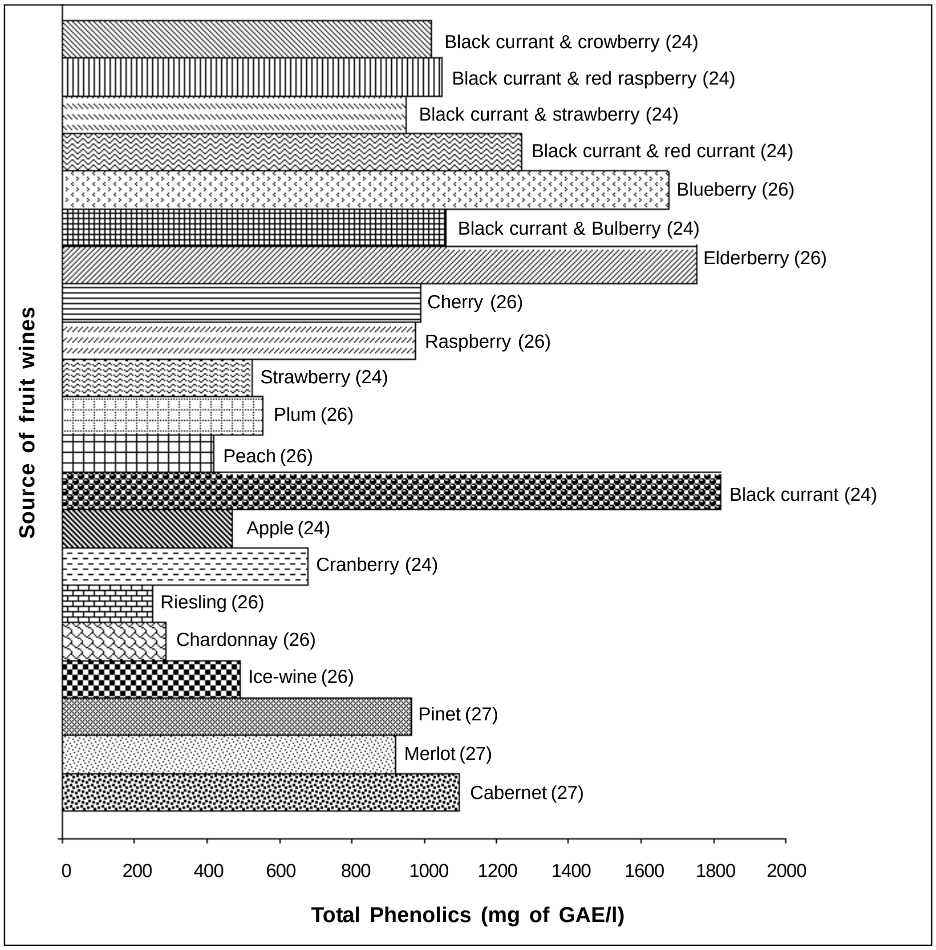
Table 1 : Oxygen Radical Absorbance Capacity (ORAC) of selected fruits

Fruits	H-ORAC (µmoles TE/100g)	L-ORAC (µmoles TE/100g)	Total Phenolics (mg GAE/ 100g)
Apricot	1108	32	79
Black berries	5245	103	660
Blue berries	6520	36	531
Cherries (sweet)	3348	17	339
Chokeberries	15820	242	2010
Cranberries	9382	202	718
Black currants	10060	84	1330
Red currants	3260	127	540
Elderberries	14500	197	1950
Red grapes	1260	-	177
Orange	1785	34	337
Pear	2941	-	168
Plum	6241	17	367
Raspberries	4745	138	502
Strawberries	3541	36	368
Bananas	813	66	230
Mango	988	14	266
Peach	1781	50	148

H-ORAC= Hydrophilic-Oxygen Radical Absorbance Capacity; L-ORAC= Lipophilic- Oxygen Radical Absorbance Capacity; Reference[22]

Flavonoids

During the past decade, flavonols have received much attention due to their plausible benefits on human health. The



Reference[24, 26, 27]

Fig. 1 : Total phenolic content of wines of different fruit sources

antioxidative, antiplatelet aggregation, anti-inflammatory, antimutagenic, anticarcinogenic and antiviral activities of quercetin and other flavonols have been demonstrated *in vitro*[32-34]. Epidemiological studies indicate that high consumption of flavonol-rich foods and beverages may be protective against CHD stroke, lung cancer and stomach cancer[35-39]. In accordance with the previous studies on grape wines the amounts of the most important flavonols in wine i.e., myricetin and quercetin, varied considerably in both the berry wines and grape wines as analyzed by Vuorinen *et al*[40-46]. The total flavonoid (given as sum of myricetin, quercetin and kaempferol content) in mg/l was estimated and was found to be in the range of 16.3-31.2 for red wines (Cabernet and Merlot) and those from black currant 10.4-34.5.

It was interesting to note that the total flavonoid and the individual myricetin and quercetin content was higher in wines from black currant and wines from black and red currant, from black currant and strawberry, black currant, raspberry and strawberry (Table 2). Another point to be noted from this extensive study is that in wines made from black currants grown in Finland, the amounts of these polyphenols with multiple biological activities were similar to those in wines produced with modern vinification techniques from Cabernet or Merlot grapes grown in the warm and sunny climates of Australia, California, or Chile[46].

In addition to flavonols, berry wines also contain other phenolic compounds such as anthocyanins, catechins, hydroxycinnamic acids and other phenolic acids and these substances are likely to make a significant contribution to the antioxidant activity and other biological activities of berry wines[47].

Antioxidant activity

Antioxidant functions are associated with lowered DNA damage, diminished lipid peroxidation or inhibited malignant transformation *in vitro*, further, they are associated epidemiologically with lowered incidence of certain types of cancer and degenerative diseases such as ischemic heart disease and cataracts. Thus along with the total phenolic content, the actual measurement of antioxidant activities can serve as a good yardstick for assessment of therapeutic value of the fruit wines. Antioxidant potential can be measured by different assay systems like MeLo oxidation, FRAP assay and ORAC assay. Each assay has its advantages and weak point and different labs have reported antioxidant activity of fruit wines using different methods.

Methyl linoleate (MeLo) is a commercially available substrate widely used for studying the inhibitory properties of pure compounds and plant extracts against lipid oxidation. In the work by

Heinonen *et al*[24] oxidation of MeLo was used to compare the antioxidant activity of the different wines. Their study showed that extracts of dealcoholized berry and fruit wines made of mixtures of black currants with crowberries or bilberries and mixtures of black and red currants and wines from raw materials such as apple, arctic bramble, crowberries, cranberries, or rowanberries possess antioxidant activity in a bulk lipid (MeLo) model. Wines made of mixtures of black currants and crowberries or bilberries were superior to other berry and fruit wines as well as to the reference red wines and equally as active as α-tocopherol in inhibiting hydroperoxide formation.

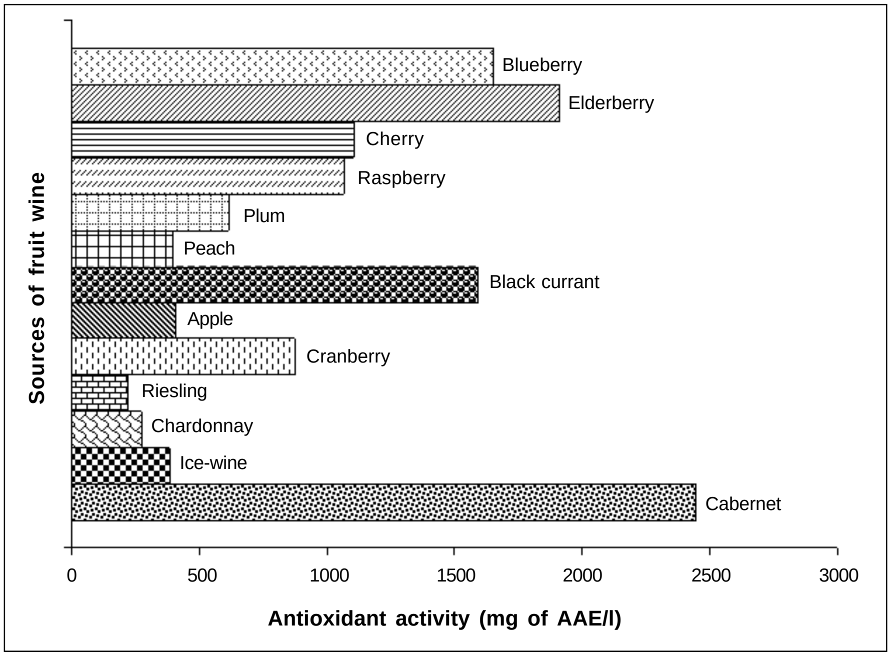
In a more recent study total antioxidant capacity (TAC) in some fruit wines was determined using the ferric reducing ability of plasma (FRAP) assay[26,48]. The FRAP assay was modified in Rupasinghe's report to express the TAC in ascorbic acid equivalents (AAE). The results of the study showed that antioxidant activity of elderberry, blue berry and black currant wines were a little less than the control red wine (Fig. 2). However, unlike the earlier study and Rupasinghe and Clegg reported that TAC of wines strongly correlated to the total phenolics[24, 26].

Some very significant facts have come into light from the study by Pinhero and Paliyath[49]. It appears that even though the relative levels of alcohol was same in blue berry and red wine, the degree of superoxide scavenging was different between the wines which suggested variations in phenolic content. Superoxide scavenging capacity of summer cherry, black berry and blue berry wines were identical. The most revealing point was

Table 2 : Flavonoid contents of different fruit wines (mg/l)

Sources of fruit wine	Myricetin	Quercetin	Kaempferol	Sum
Cabernet	9.5 ± 0.1	6.7±0.1	<1.2	16.3
Merlot	11.8±0.3	19.4±0.6	<1.2	31.2
Black currant	22.6 ±0.6	11.9 ±0.2	<1.2	34.5
Black currant	14.6 ±0.1	8.8±0.0	<1.2	23.5
Black currant	14.5 ± 0.2	8.7 ±0.1	<1.2	23.1
Black currant	11.2±0.0	9.8 ±0.0	2.1 ± 0.0	23.0
Black currant	13.2±0.1	8.3±0.1	<1.2	21.5
Black currant	7.3 ±0.1	3.1 ±0.0	<1.2	10.4
Black currant, red currant	10.3 ± 0.3	6.7 ±0.1	<1.2	17.0
Black currant, strawberry	10.5 ± 0.4	11.1 ± 0.4	3.3±0.1	24.9
Black currant, raspberry, strawberry	14.8 ±0.2	8.5±0.1	<1.2	23.3
Black currant, crowberry	13.0 ± 0.1	10.2±0.0	<1.2	23.3
Black currant, crowberry	6.5±0.1	4.0±0.1	<1.2	10.5
Black currant, crowberry	5.7±0.0	3.7 ± 0.0	<1.2	9.4
Black currant, crowberry	4.8±0.2	3.0 ± 0.2	<1.2	7.8

Reference[46]



Reference[46]

Fig. 2 : Total antioxidant activity of fruit wines

that on the basis of specific phenolic content, the cherry, black berry and blue berry wines were 30-40% more efficient in superoxide radical scavenging than red grapes. Hydroxyl radical-scavenging capacity was also estimated in the same study. Phenolic components from blueberry and summer cherry were more effective in hydroxyl radical scavenging than those of blackberry or red wine.

Recently Yildirim[25] evaluated the antioxidant activities of fruit wines and arranged them in the following order bilberry>blackberry>black mulberry>sour cherry> strawberry> raspberry>apple>quince>apricot>melon.

Studies have been performed on relationships of phenolic content and their contribution to antioxidant activities in different fruit wines. With respect to fruit wines especially berry wines, Heinonen *et al*[24] found that all the wines studied possessed significant antioxidant activity, but there was no strict correlation between the content of phenolic components and antioxidant activity. However, other workers have reported a strict positive correlation between the polyphenol content and antioxidative effect[26,49,50]. The contradictory results could be attributed to differences in evaluating the antioxidant function.

Thus contradictory results in the correlation between total phenolics and antioxidant activity of fruit wines can be explained. Many fruits and berries contain significant amounts of anthocyanins compared to other flavonoids, markedly less flavan-3-ols and generally less hydroxycinnamic acids than grapes[51]. According to Singleton[52] anthocyanins respond poorly in the Folin-Ciocalteu assay, their response being 0.40 compared to the 1.00 and 0.99 responses of gallic acid and catechin, respectively. Therefore, the total phenolic content, i.e. the reducing capacity of berry and fruit wines, does not accurately respond to the true antioxidant nature of their phenolic constituents. Grape wines, on the other hand, are especially rich in gallic acid and catechin. Moreover, the lack of correlation between the total phenolic content and the antioxidant activity of berry and fruit wines may also be explained in part by the wide range of raw materials differing significantly in their composition of phenolic compounds.

Irrespective of the contradictory results, the presence of phenolics and the antioxidant capacity of fruit wines can not be doubted. Since, each phenolic group differs with regard to its own antioxidant potency, these differences may result in variation in the antioxidant capacity of each wine.

Elemental composition of fruit wines

As more attention is being paid to the nutritional aspects of beverages like wine, interesting facts are coming to our knowledge. For example, the recent study by Rupasinghe and Clegg[26] also reported a comparative analysis of different elements in fruit wines (Table 3). It appears that cranberry wine has the highest content of calcium as compared to other fruit wines and black currant wine has the highest content of potassium. Another important mineral Fe, was found to be 3 to 4 times higher in cranberry and black currant wines as compared to red wine. However, one has to keep in mind that the influence of factors such as geographical environment, soil chemistry, viticultural practices and processing methods would most definitely influence the elemental composition of

Table 3 : Elemental composition (µg/g) of selected categories of wines of different fruit sources

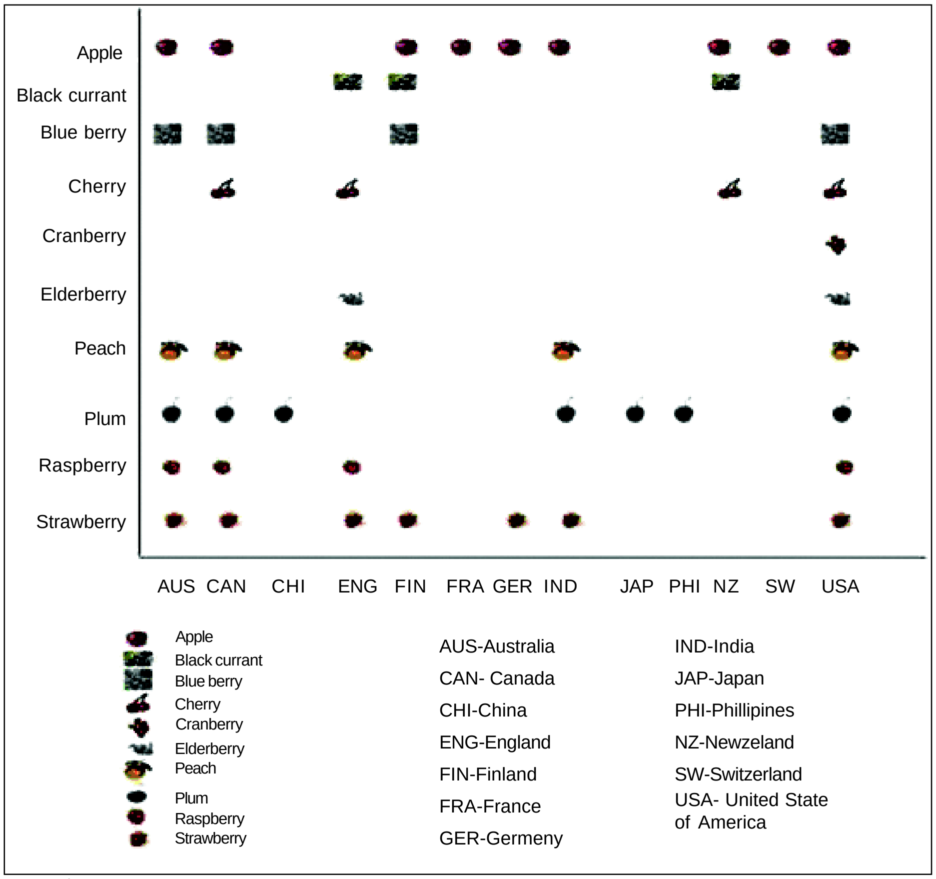
Sources of fruit wine	Ca	K	Mg	Na	P	S	Fe	Mn	Zn
Cabernet	62	956	108	48	157	140	0.9	2.6	0.8
Chardonnay	62	632	349	52	201	160	1.3	1.9	0.7
Cranberry	643	791	43	48	120	99	4.5	1.5	0.4
Apple	45	958	38	31	68	80	0.4	0.2	0.2
Black currant	108	1201	45	33	102	81	3.2	1.0	0.5
Raspberry	96	742	67	42	64	80	0.5	0.5	0.5
Cherry	69	834	50	38	54	136	1.2	0.2	0.1
Elderberry	89	831	106	62	149	171	1.2	0.9	0.2
Blueberry	96	958	82	63	75	113	0.6	14.6	0.5

Reference[26]

fruit wines. Another significant observation of this study was that biogenic amine that putatively causes headache, histamine, is present only in low amounts (41-224µg/l) in fruit wines like pear, cranberry, peach, black currant, elderberry, blue berry as compared to red wines (11,143µg/l)[26] further strengthening the theory that fruit wines may be considered healthful and in some cases better than red wines.

Market potential

In the light of scientific proof of health benefits from fruits like berries there seems to be steady growth of worldwide market for fruit wines. Figure 3 shows some of the countries which are marketing different fruit wines[53]. However, it would also be wise to remember that the health promoting capacity of these fruit wines will depend on number of factors like the environment in which the fruits are grown and the time of maceration and fermentation in contact with the fruit skins, pressing and maturation, finning, bottling and ageing. The steadily growing data that demonstrates the presence of flavonoids, phenolics and antioxidant potency of many fruit wines can be a great impetus on technological approaches that could be adopted for improvement of the nutraceutical properties of fruit wines. The colour and therapeutic properties of the wine is due to the presence of flavonoid and their derivatives and any technique that would result in extraction of these compounds during wine making will improve the nutraceutical qualities of wines and make them "functional". It would also be prudent to explore other fruits which have been hitherto underexplored by the wineries.



Reference[53]

Fig. 3 : Some of the countries selling fruit wines

Conclusions

To consider a food as 'functional', it should have high levels of nutraceutical compounds that will have physiological effects. In this context some of the studies reviewed in this article point out unambiguously that fruit wines do have the nutraceutical compounds with experimentally proven antioxidant potential. Based on this, it would not be unjustified to conclude that the relative content of these antioxidants in fruit wines may provide added value to the wines and that the "functional" status can be conferred on fruit wines, especially from berries, based on the presence of antioxidants. However, a lot of effort still needs to be focused in finding ways to control their occurrences in these wines. Moreover, the protective effects of berry wines on human health as well as the role of flavonols and other polyphenolic constituents remain to be elucidated. In order to make fruit wines with nutraceutical value, the agricultural practices for growing the fruit and the processing method to convert the fruits in to wines needs to be understood.

References

1. Leach HM, Popular diets and anthropological myths, *N Z Med J*, 1989, **102**, 474-477.

2. Hasler CM, Functional foods: the western perspective, *Nutr Rev,* 1996, **54**(suppl), 6S-10S.

3. Glinsmann WH, Functional foods in North America, *Nutr Rev,* 1996, **54** (suppl), 33S-37S.

4. Clydesdale FM, A proposal for the establishment of scientific criteria for health claims for functional foods, *Nutr Rev*, 1997, **55**, 413-422.

5. Thomas PR and Earl R, Committee on Opportunities in the Nutrition and Food Sciences, Institute of Medicine, Opportunities in the nutrition and food sciences: research challenges and the next generation of investigators, PR Thomas and R Earl (Editors), Washington, DC: National Academy Press, 1994, 109-142.

6. Renaud SC and De Lorgeril M, Wine, alcohol, platelets and the French paradox for coronary Heart disease, *Lancet*, 1992, **339**, 1523-1526.

7. Frankel E, Kanner J, German JB, Parks E and Kinsella JE, Inhibition of oxidation of human low-density lipoprotein by phenolic substances in red wine, *Lancet*, 1993, **341**, 454-457.

8. Teissedre PL, Frankel EN, Waterhouse AL, Peleg H and German JB, Inhibition of *in vitro* human LDL oxidation by phenolic antioxidants from grapes and wines, *J Sci Food Agric*, 1996, **70**, 55-61.

9. Stoclet JC, Kleschyov A, Andriambeloson E, Dielbolt M and Andriantsitohaina R, Endothelial NO_3 release caused by red wine polyphenols, *J Physiol Pharmacol*, 1999, **50**, 535-540.

10. Mattace Raso G, Meli R, Di Carlo G, Pacilio M and Di Carlo R, Inhibition of inducible nitric oxide synthase and cyclooxygenase-2 expression by flavonoids in macrophage J774A, *Life Sci*, 2001, **68**, 921-931.

11. Fauconneau B, Waffo Teguo P, Huguet F, Barrier L, Decendit A and Merillon JM, Comparative study of radical scanvenger and antioxidant properties of phenolic compounds from *Vitis vinifera* cell cultures using *in vitro* tests, *Life Sci*, 1997, **61**, 2103-2110.

12. Pace-Asciak CR, Hahn S, Diamandis EP, Soleas G and Goldberg DM, Wines and grape juices as modulators of platelet aggregation in healthy human subjects, *Clin Chem Acta*, 1995, **235**, 207-219.

13. Varache-Lembege M, Waffo-Teguo P, Richard T, Monti JP, Deffieux G, Vercauteren J, Merillon JM and Nuhrich A, Structure-activity relationships of polyhydroxystilbene derivatives extracted from *Vitis vinifera* cell culture as inhibitors of human platelet aggregation, *Med Chem Res*, 2000, **10**, 253-267.

14. Clifford AJ, Ebeler SE, Ebeler JD, Bills ND, Hinrichs SH, Teissedre PL and Waterhouse AL, Delayed tumor onset in transgenic mice fed an amino acid-based diet supplemented with red wine solids, *Am J Clin Nutr*, 1996, **64**, 748-756.

15. Joshi VK, Sandhu DK and Thakur NK, Fruit based alcoholic beverages, *In*: Biotechnology: Food Fermentation, Vol 2 by VK Joshi and A Pandey (Editors), Educational Publishers and Distributors, Kerala, India, 1999, pp. 647-744.

16. Schmidt DR and Sobota AE, An examination of the antiadherence activity of cranberry and low-density lipoprotein oxidation, *Ann Nutr Metab*, 1998, **41**, 353-357.

17. Hakkinen S and Auriola S, High-performance liquid chromatography with electrospray ionization mass spectrometry and diode array ultraviolet detection in the identification of flavonol aglycones and glycosides in berries, *J Chromatogr A,* 1998, **829**, 91-100.

18. Hakkinen SH, Karenlampi SO, Heinonen IM, Mykkanen HM and Torronen AR, HPLC method for screening of flavonoids and phenolic acids in berries*, J Sci Food Agric* 1998, **77**, 543-551.

19. Hakkinen S, Heinonen M, Karenlampi S, Mykkanen H, Ruuskanen J and Torronen R, Screening of selected flavonoids and phenolic acids in 19 berries*, Food Res Int*, 1999a, **32**, 345-353.

20. Hakkinen SH, Karenlampi SO, Heinonen IM, Mykkanen HM and Torronen AR, Content of the flavonols quercetin, myricetin and kaempferol in 25 edible berries*, J Agric Food Chem,* 1999b, **47**, 2274-2279.

21. Kahkonen MP, Hopia AI and Heinonen M, Berry phenolics and their antioxidant activity, *J Agric Food Chem*, 2001, **49**(8), 4076-4082.

22. Bhagwat S, Haytowitz DB and Holden JM, American Institute for Cancer Research Launch Conference, November 1-2, 2007, Washington, DC.

23. Kanner J, Frankel E, Granit R, German B and Kinsella JE, Natural Antioxidants in Grapes and Wines, *J Agric Food Chem*, 1994, **42**, 64-69.

24. Heinonen M, Lehtonen PJ and Hopia AI, Antioxidant activity of berry and fruit wines and liquors, *J Agric Food Chem*, 1998, **46**, 25-31.

25. Yildirim HK, Evaluation of colour parameters and antioxidant activities of fruit wines, *Int J Food Sci Nutr*, 2006, **57**(1/2), 47-63.

26. Rupasinghe HPV and Clegg S, Total antioxidant capacity, total phenolic content, mineral elements and histamine concentrations in wines of different fruit sources, *J Food Comp Anal*, 2007, **20**, 133-137.

27. Mazza G, Fukomoto L, Delaquis P, Girard B and Ewert B, Anthocyanins, Phenolics, and color of Caberbet Franc, Merlot and Pinot noir Wines from British Columbia, *J Agric Food Chem*, 1999, **47**, 4009-4017.

28. Zeb A, Important therapeutic uses of Sea buckthorn (Hippophae): A Review, *J Biol Sci*, 2004, **4**(5), 687-693.

29. Cheng J, Kondo K, Suzuki Y, Ikeda Y, Meng X

and Umemura K, Inhibitory effects of total flavones of *Hippophae rhamnoides* Linn. on thrombosis in mouse femoral artery and *in vitro* platelet aggregation, *Life Sci*, 2003, **72**, 2263-2271.

30. Dienr HC and Ringleb P, Antithrombotic secondary prevention after stroke, *Curr Treatm Option Neurol*, 2001, **3**, 451-62.

31. Negi B and Dey G, Comparative analysis of total phenolic content in Sea buckthorn wine and other selected fruit wines, Paper accepted for International Conference of Biotechnology and Food Engineering, Paris, June 24-26th, 2009.

32. Formica JV and Regelson W, Review of the biology of quercetin and related bioflavonoids, *Food Chem Toxicol,* 1995, **33**, 1061-1080.

33. Hertog MGL and Hollman PCH, Potential health effects of the dietary flavonol quercetin, *Eur J Clin Nutr,* 1996, **50**, 63-71.

34. Soleas GJ, Diamandis EP and Goldberg DM, Wine as a biological fluid: History, production and role in disease prevention, *J Clin Lab Anal,* 1997a, **11**, 287-313.

35. Hertog MGL, Feskens EJM, Hollman, PCH, Katan MB and Kromhout D, Dietary antioxidant flavonoids and risk of coronary heart disease: The Zutphen Elderly Study, *Lancet,* 1993a, **342**, 1007-1011.

36. Hertog MGL, Kromhout D, Aravanis C, Blackburn H, Buzina R, Fidanza F, Giampaoli S, Jansen A, Menotti A, Nedeljkovic S, Pekkarinen M, Simic BS, Toshima H, Feskens E JM, Hollman PCH and Katan MB, Flavonoid intake and long-term risk of coronary heart disease and cancer in the Seven Countries Study, *Arch Intern Med*, 1995, **155**, 381-386.

37. Hertog MGL, Feskens EJM and Kromhout D, Antioxidant flavonols and coronary heart disease risk, *Lancet,* 1997, **349**, 699.

38. Knekt P, Jarvinen R, Reunanen A and Maatela J, Flavonoid intake and coronary mortality in Finland: a cohort study, *Brit Med J,* 1996, **312**, 478-481.

39. Keli SO, Hertog MGL, Feskens EJM and Kromhout D, Dietary flavonoids, antioxidant vitamins and incidence of stroke: The Zutphen study, *Arch Intern Med,* 1996, **156**, 637-642.

40. Knekt P, Jarvinen R, Seppanen R, Heliovaara M, Teppo L, Pukkala E and Aromaa A, Dietary flavonoids and the risk of lung cancer and other malignant neoplasms, *Am J Epidemiol,* 1997, **146**, 223-230.

41. Garcia-Closas R, Gonzalez CA, Agudo A and Riboli E, Intake of specific carotenoids and flavonoids and the risk of gastric cancer in Spain, *Cancer Causes Contr,* 1999, **10**, 71-75.

42. Hertog MGL, Hollman PCH and van de Putte B, Content of potentially anticarcinogenic flavonoids of tea infusions, wines and fruit juices, *J Agric Food Chem,* 1993b, **41**, 1242-1246.

43. Frankel EN, Waterhouse AL and Teissedre PL, Principal phenolic phytochemicals in selected California wines and their antioxidant activity in inhibiting oxidation of human low-density lipoproteins, *J Agric Food Chem,* 1995, **43**, 890-894.

44. Justesen U and Knuthsen P, The use of HPLC and mass spectrometry for the determination of flavonoids in red wines, Polyphenol Communications 98, XIXth International Conference on Polyphenols, 1998, 377-378.

45. McDonald MS, Hughes M, Burns J, Lean MEJ, Matthews D and Croziers A, Survey of the free and conjugated myricetin and quercetin content of red wines of different geographical origins, *J Agric Food Chem*, 1998, **46**, 368-375.

46. Vuorinen H, Mtt K and Trrnen R, Content of the Flavonols Myricetin, Quercetin, and Kaempferol in Finnish Berry Wines, *J Agric Food Chem*, 2000, **48**(7), 2675-2680.

47. Lehtonen PJ, Rokka MM, Hopia AI and Heinonen IM, HPLC determination of phenolic compounds in berry and fruit wines and liquers, *Wein Wissensch Viticult Enol Sci*, 1999, **54**, 33-38.

48. Benzie IFF and Strain JJ, The ferric reducing ability of plasma (FRAP) as a measure of "antioxidant power": the FRAP assay. *Anal Biochem*, 1996, **239**, 70-76.

49. Pinhero RG and Paliyath G, Antioxidant and calmodulin in hibitory activities of phenolic components in fruit wines and its biotechnological implications, *Food Biotech*, 2001, **15**(3), 179-192.

50. Abu-Amsha R, Croft KD, Puddey IB, Proudfoot JM and Beilin LJ, Phenolic Content of Various Beverages Determines the Extent of Inhibition of Human Serum and Low-density Lipoprotein Oxidation *in vitro*: Identification and Mechanism of Action of Some Cinnamic Acid Derivatives from Red Wine, *Clin Sci*, 1996, **91**, 449-458.

51. Macheix JJ, Fleurit A and Billot J, Flavonoids, *In*: Fruit Phenolics; CRC Press: Boca Raton, FL, 1990, 39-80.

52. Singleton VL, Analytical fractionation of the phenolic substances of grapes and wine and some practical uses of such analyses, *In*: Chemistry of winemaking, Webb, AD, ED, American Chemistry Society, Washington, DC, 1974.

53. www.bowersharbor.com; www.winegardenestate.com/index.htm