ISSN PRINT 2319 1775 Online 2320 7876

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Cherries: A Treasure Of Bioactive Compounds With Promising Health Promoting Functional Potential

Abid Ali Sheikh[1*], Lacy Loveleen[2], Kushal Kant Pant[3], Vikas Chandra[3*]

[1]National Institute of Biologicals (NIB), Sector-62, Noida, Uttar Pradesh, Pin 201309, India
[2]Department of Biotechnology, Central University of Rajasthan (CURAJ), Ajmer, Rajasthan, Pin 305817, India
[3]Department of Biotechnology, Guru Ghasidas Vishwavidyalaya, Bilaspur, Chhattisgarh, Pin 495009, India

[*]**Email Address and mobile no. of Corresponding Authors:**
Abid Ali Sheikh: abidalis2007@gmail.com, +91 7006161922
Vikas Chandra: digvijay.chandra@gmail.com, +91 7974157693

ABSTRACT

Cherries are drupe fruits that are categorized under the genus *Prunus* andthe family Rosaceae. Although their different species are extensively used worldwide, the commercial cherries are categorized into two species i.e. *Prunus cerasus* (tart/sour cherry) and *Prunus avium* (sweet cherry). The cherries harbour various phytochemicals such as polyphenols, flavonoids, and anthocyanins in their fruits, leaves, and stems. Due to their phytochemical constituents, cherries can be utilized as anti-inflammatory, antioxidant, antidiabetic, and anti-aging foods. Apart from this, cherries are also used to treat cancers, arthritis, and neurological disorders. Moreover, Cherries are used as functional foods as they contain some nutritional elements (such as potassium) and organic molecules (such as amino acids, vitamin C, carotenoids, melatonin and dietary fibers). The sour cherry (*Prunus cerasus*) is found to be more effective in disease treatment and is rich in medicinal properties than sweet cherry (*Prunus avium*). A significant increase in production of sour as well as sweet cherries has been observed due to their increased consumption owing to their varied nutritional and medicinal properties. In this review, we have included the different therapeutic and functional properties of *Prunus avium* and *Prunus cerasus* along with few other species of cherries with relevant studies performed to evaluate their pharmacological properties. Mechanistically, cherries exhibit relatively high antioxidant activity, low glycemic response, COX 1 and 2 enzyme inhibition, and other anti-carcinogenic effects in vitro and in animal experiments. Well-designed cherry feeding studies are needed to further substantiate health benefits in humans.

Keywords: Anthocyanin, Antioxidant, Flavonoid, Polyphenol, *Prunus avium*, *Prunus cerasus*

ISSN PRINT 2319 1775 Online 2320 7876

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INTRODUCTION

Many medicinal plants, herbal drugs and fruits have been studied for their immunopharmacological activities. Various epidemiological studies have shown that incorporation of plant based foods such as fruits and vegetables in diet in balanced quantities can find ways to cure chronic ailments e.g. diabetes, some types of cancers, various inflammatory diseases and cardiovascular diseases. A combined cure to various diseases is because of phytochemicals present in plant based foods that not only provide vitamins and minerals for various enzymatic reactions inside the body, but can also contribute to the production of polyphenol[1]. These phenolic compounds have ability to act as scavengers of oxygen containing reactive species (ROS) that are responsible for damaging multiple organs in human bodies. Other than these, many traditional medicines are also known to have potential immunomodulatory effect on our immune system[2].

Humans have been using fruits as functional foods from very ancient time. The fact is that they are delicious, easily digestible, and nutritious and are thought to cure many diseases. Advancement in science has led us to discover the hidden medicinal properties of fruits. One major genus category, the members of which are being consumed as superfruits, is *Prunus*, consumed by humans for centuries. Owing to their medicinal as well as economic values cherries are cultivated in large scale. A number of berries and drupe or stone fruits fall into the genus *Prunus*, but mainly *Prunus cerasus* (sour/tart cherries) take the opportunity to serve us with maximum health benefits[3]. The use of cherries has increased extensively in past decades and hence their productivity and economic value also increased. Among several species of the genus *Prunus*, the two most important species of cherry are *Prunus cerasus* (tart/ sour cherry) and *Prunus* avium (sweet cherry).

This review summarizes different chemical, biological, functional and some of the technical characteristics of cherry plants and their uses all over the world. We have also tabulated relevant studies and their outcomes.

Two Widely Used Categories of Cherry: Sour and Sweet

Based on the taste of cherry fruits, they are roughly categorized as sour/tart cherries (*Prunus cerasus*) and sweet cherries (*Prunus avium*). The taste of cherries may vary as per the cultivar, portion of fruit, storage, stage of ripening and their phenolic content as well. Tart and sweet cherry are known to carry numerous compounds that are extensively supposed to have health related benefits. The most common characteristic of cherries is their antioxidant property that has extended their utilizations as free radical scavengers, anti-diabetic, anti-inflammatory, and anti-ageing agents etc. Reports from various scientific studies revealed much more than just the above-mentioned properties. Some of them suggest the role of cherry extracts in treatment of chronic disorders including cancers, arthritis, diabetes, and also some of the neurological disorders.

Cherries belong to the family Rosacea and the genus *Prunus*. Scientific classification of *Prunus*[4] is given in table 1.

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Table 1: Scientific classification of *Prunus*

Taxonomic rank	Classification
Kingdom	Plantae
Subkingdom	Tracheobionta
Superdivision	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Rosidae
Order	Rosales
Family	Rosaceae*
Subfamily	Prunoideae
Genus	*Prunus*

(Source: USDA)

Habit and Habitat of Cherries

There are several varieties of cherry found in different locations, but usefulness, productivity, and economic values of sour cherries (*Prunus cerasus*) are incomparable, followed by sweet cherries (*Prunus avium*).

The sour cherry is medium sized tree (shrub) with more spreading habit, smaller than the erect sweet cherry (*Prunus avium*) and is more tolerant of extremes in temperature. The trees may reach 10 meters in height, with a trunk diameter of 30 to 45 cm. The flowers are white to pale pink, bark is grayish-brown in colour, and leaves are ovate with serrated edging. Sour cherry fruits can grow up to 20 mm in length and 18 mm in width. They are cordate drupes, with colour ranging from light to dark red. Such fruits envelop light brown seed[5]. The sweet and tart cherry do not have very much difference in their morphology. The trees of sweet cherry (*Prunus avium*) are relatively taller, compared to sour cherry, with height up to 15 meters. The barks of sweet cherries are gray-brown in colour. Leaves of sweet cherries are oval in shape. They harbor white clustered flowers which appear in early springs. The Fruits are dark red which mature in mid of summer[6].

Cherries are native to most parts of Europe and South-West Asia. In India, they are being cultivated in northern regions of the country (Jammu and Kashmir and Himachal Pradesh). But the productivity depends on various environmental factors such as climatic condition, soil microbes and soil texture, water availability, temperature etc. Due to this reason, some of the places where cherries are easily grown have advantages over other regions both in terms of availability and economy. Sour cherry, morello cherry, tart cherry, and pie cherry are grown in different regions of the world with different names[5].

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Phytochemical Constituents of Cherries

Cherries are low calorie containing fruits, enriched with various nutrients, amino acids, and bioactive compounds such as fibers, vitamins C, potassium, polyphenols, carotenoids, serotonin, and tryptophan. They also contain a wide array of antioxidants and other phytonutrients (including melatonin, kaempferol, chlorogenic acid, p-coumaric acid, gallic acid, perillyl alcohol and ellagic acid etc[7]. Cherries contain a number of phenolic compounds, more specifically anthocyanin pigments that not only provide cherry with its colour and sweet and sour taste, but also are responsible to impart all medicinal properties present in cherries. Besides fruits, other parts like stalks, seeds and barks of cherry are also used for medicinal and cosmetic applications. They can be utilized as relaxant, astringent, detoxicant, and as treatment for some of the bacterial and viral diseases. Leaves of cherry are used to extract a green colour dye that is used as natural food coloring agent. An infusion of sour cherry leaves is given for convulsions in children. The kernels of cherries contain a significant amount of hydrocyanic acid. The leaves carry amygdalin which is a nitrile glycoside compound with anticancer activity[8].

Nutritional and Medicinal Values of Sour/ Cherries (*Prunus cerasus*)

Tart cherries are comparatively more sufficient in nutritional values such as polyphenols, flavonoids and anthocyanins and hence included as functional food in our diet. In particular, red cherries are used in traditional herbal remedies for various diseases such as dropsy, beriberi, heart failure, mastitis etc. The role of *P. cerasus* to modulate a variety of biological responses has been constantly reported. It has been extensively used in many indigenous nutraceutical preparations owing to its medicinal values and different pharmacological actions such as, anti-arthritic, cardio-protective, anti-inflammatory, anti-cancer, anti-diabetic and anti-aging properties. Moreover, it has the potential to be used for the treatment of retinopathy, neurological disorders, weight management, and muscle recovery.

Tart cherries produces various kinds of phenolics and polyphenolics, that include cyanidin derivatives, peonidin 3-glucoside, isorhamnetin, quercetin, kaempferol, chlorogenic-, gallic-and, p-coumaric- acid, daidzein and rutin, ellagic acid, melatonin and alkaloids. These active compounds are being called "Mother Nature's all-natural chemotherapy agents"[9]. Wang *et al.*, isolated three novel antioxidant compounds as (1):2-hydroxy-3-(*o*-hydroxyphenyl) propanoic acid, (2):1-(3′,4′-dihydroxycinnamoyl)-cyclopenta-2,5-diol, and (3): 1-(3′,4′-dihydroxycinnamoyl) cyclopenta-2,3-diol, determined by their spectral data from ethyl acetate (EtOAc) extract of *Prunus cerasus*[10].

The phenolic content of sour cherries is known to safeguard neuronal cells from cellular damages caused by oxidative stress and may lower the risk of cancer and hence should be consumed in high amount. In a study, the effect of sour cherry juice was observed on normal rats and rats suffered from hyperuricemia. This study revealed that there is a significant reduction in serum uric acid level in hyperuricemic rats while no significant reduction was observed in normal rats. Moreover, *Prunus cerasus* juice leads to inhibition of

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liver xanthine oxidase/dehydrogenase activities and cause a significant increment in serum total antioxidant capacity in normal as well as hyperuricemic rats. These features of *Prunus cerasus* make it suitable candidate for prophylactic treatment of hyperuricemia, particularly if to be consumed on a long-term basis[11]. Isobolographic analysis revealed the 3kinds of interactions i.e. synergistic, additive, and negative interactions among diverse phytochemicals and concluded that not all polyphenols in sour cherry fruits are equally effective in alleviating oxidative stress and the most effective interaction is the one that occurs through synergic interactions[12].

Nutritional and Medicinal Values of Sweet Cherries (*Prunus avium*)

Sweet cherry fruit contains an adequate level of free radical scavengers such as phenolic acids and flavonoids. Due to this, fruit extracts show good antioxidant properties. The stem of sweet cherry shows more antioxidant potential compared to fruit extracts, and higher phenolic compound concentration is obtained in stem extracts than fruit. One study revealed antitumor property of fruit extracts against HCT-15 colon carcinoma cell lines. This could be due to anthocyanin which is only present in fruits but not in stems[13]. Dziadek et al., found that sweet cherry leaves provide adequate amount of dietary fibers, vitamin C, and carotenoids. They also found that these compounds are higher in leaves than petiole and fruit. They also observed free radical scavenging activity of sweet cherry extracts[14]. When *Prunus avium* alcoholic extracts were tested for *in vitro* sperm activation, they were able to enhance sperm parameters[15]. The leaves methanolic extracts of sweet cherries inhibit DNA damage by free radicals as it exhibits free radical scavenging activity[16]. It has been also deduced that the stem extracts of sweet cherries have good anti-aging properties[17]. Jacob et al., found that sweet cherry consumption decreases plasma urate, indicating that cherries can be used to treat gout[18].

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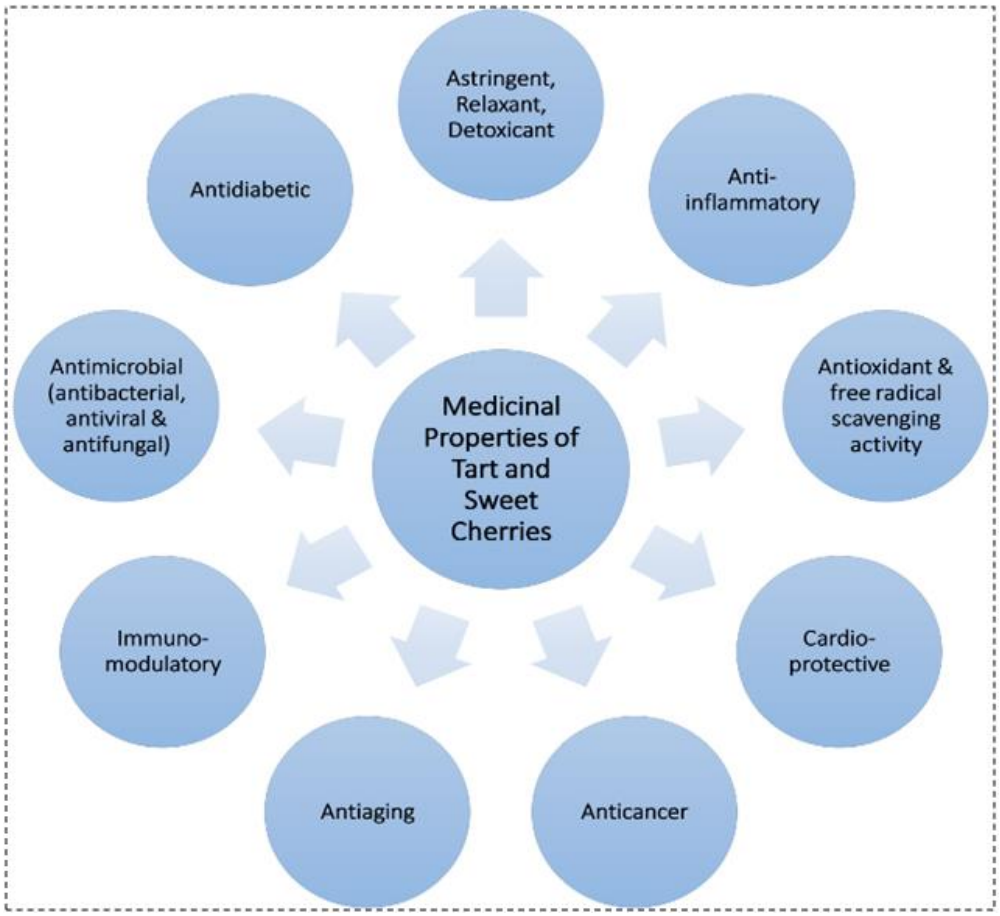

Figure 1: Important medicinal properties of *P. cerasus* (sour cherry) and *P. avium* (sweet cherry)

Relevant Studies and Their Outcomes

Table 2 summarizes relevant studies and their outcomes concerned with phytochemical, pharmacological, biological, functional and some of the technical characteristics of cherry plants (especially sour and sweet cherries) and their uses all over the world.

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Table 2: Phytochemical and Pharmacological evaluation and some other parameters of cherries

Plant source/ Parts used	Extracts/fractions/ compound (s) used	Biological activities/ parameters tested	Result reproduced	References
Prunus avium	Non-extractable polyphenols (NEPs) from cherry pomace	Enzyme assisted extraction method was developed for the extraction of NEPs.	Higher amount of proanthocyanidins and phenolic contents were extracted than alkaline acid hydrolysis methods.	[19]
Prunus avium	Stem extract of *Prunus avium*	Anti-ageing property of three new extracts of sweet cherry obtained using green-extraction techniques (pressurized solvent, supercritical CO_2, and subcritical water extractions) was assessed.	Anti-ageing properties such as antioxidant capacity, especially against lipid peroxyl and •OH free radicals. Highest anti-ageing activity was shown by stem extract obtained using supercritical CO_2 extraction technique.	[17]
Prunus avium	Kernel oil of 4 varieties of *P. avium* (i.e. *Burlat, Napol-eon, Coeurde pigeon, Van*) extracted in N-hexane	Comparative study and characterisation of four varieties of *Prunus avium* kernel oil.	High amount of active compounds: linoleic and oleic fatty acids, β-sitosterol, campesterol and δ-(5)-avenasterol and tocopherols were obtained in kernel oil. Overall oil yield was highest in "*Coeur de pigeon*" variety.	[20]

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Prunus cerasus	Fruit methanolic extract	Phenolic and flavonoids content in sour cherry methanolic extract was measured. Antioxidant potential of the extract was also evaluated	The extract showed high antioxidant potential and being at reassure of bioactive compounds: polyphenols, flavonoids and anthocyanins, may prevent various diseases.	[21]
Prunus cerasifera	Leaf methanolic extract fractionated by ethyl acetate and butanol	Phenolic constituents from *P. cerasifera* leaves were extracted and identified.	Phenolic acids such as *p*-coumaric acid, caffeic acid, ferulic acid, chlorogenic acid, 3-*O*-caffeoylquinic acid, 5-*O*-coumaroylquinic acid, 3-*O*-caffeoylquinic acid methyl ester, chlorogenic acid methyl ester, 3-*O*-caffeoyl-5-*O*-coumaroylquinic- and protocatechuic-acid obtained from ethyl acetate extract.	[22]
Prunus avium	Fruit extract	Phenolics from dark sweet cherry in whole extract and fraction enriched in phenolic acids, flavonols and proanthocyanidins were assessed for its use as phytochemical therapeutics for breast cancer subtype.	Phenolic fractions enriched in anthocyanins showed strong ability to be used as chemotherapeutics for aggressive breast cancer subtype.	[23]
Prunus avium	Fruit extract	Extraction of phenolics of Royal Dawn sweet cherry was optimized using response surface method. Phenolic profile was characterised in extracts using HPLC-ESI-MS/MS.	Rutin was the most predominant phenolic compound in extract. Use of ethanol as solvent was found to decrease the extraction rate for anthocyanins.	[24]
Prunus cerasus	Methanolic fruit extract	Graded doses of methanolic fruit extract were introduced into sheep red blood cell (SRBC) immunised BALB/c mice to check its effect on immune system as well as its antioxidant activity.	The fruit extract showed immunomodulation under in vivo conditions and was able to prevent oxidative damage in immunological system.	[25]

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Prunus avium	Fruit extract	Comparative study of numerous bioactive molecules and antioxidant property found in various traditional and commercially available cultivars of sweet cherry.	Bioactive compounds (polyphenols, flavonoids, anthocyanins) were present in higher concentration in commercially available cultivars as compared to traditional cultivars. Among commercial cultivars bioactive molecules and antioxidant activities were present in high quantity in Cordia and Sylvia fruits. Among traditional cultivars highest antioxidant property was found in fruits of Black Late cherry. Antioxidant activity of extracts showed a strong positive correlation with bioactive molecules.	[26]
Prunus cerasus	Fruit extract	Co-digestion of sour cherry extract was simulated in dairy model-systems comprising milk, non-fat yoghurt, probiotic yoghurt or cream to observe change in their phytochemical property	Distinct effects were observed on bioavailability of individual sour cherry phenolics when dairy food matrix components were evaluated.	[27]
Prunus cerasus	Fruit extract	Determination of the vital nutritional qualities of cherry fruit.	Various components like sorbitol, malic acid, anthocyanins were obtained. Cyanidin 3-glucosyl rutinoside was the most abundant biomolecule in extract.	[28]
Prunus cerasus	Hydro-methanol extracts of fruit	Effect of hydro-methanol fruit extract as antidiabetic treatment. Alloxan-induced diabetic rats were used as experimental animal model for studying effect of extracts *in vivo*.	Hydromethanol extract of cherry fruits was found to exhibit remarkable antidiabetic effects.	[29]

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Prunus avium	Stick cherry extract	Effect of stick cherry extracts using three solvents: methanol, ethanol and boiling water. Preparation of silver nano-particles of stick cherry extract and observation of their effect on the inhibition zone of pathogenic bacterial growth.	Combination of aqueous and methanolic cherry extract affected only *Proteus mirabilis* and *Staphylococcus aureus*. While ethanolic extract affected *Proteus mirabilis*, *Lactobacillus*, *Staphylococcus aureus.*	[30]
Prunus avium and *Prunus cerasus*	Aqueous and aqueous-glycerin extracts from sweet and sour cherry	The phenolic compounds, L-ascorbic acid, and antioxidant potential of aqueous and aqueous glycerin extracts were evaluated to determine their potential as cleansers.	Because of very high antioxidant property, extract may be utilized as raw materials for preparation of cosmetics and cleansers.	[31]
Prunus avium	Fruit extract	Colored and non-colored fractions and total extract of Saco cherry were analyzed for their phenolic compounds using HPLC. Also, their antioxidant, anti-diabetic, erythrocyte protection, and cytotoxic action on Caco-2 cell lines were determined.	Total extracts and non-colored fractions were rich in hydroxycinnamic acids, whereas colored fractions were rich in cyanidin-3-O-rutinoside. The erythrocytes protection activity (in terms of prevention of hemoglobin oxidation and hemolysis) was effectively shown by coloured fractions. In case of Caco-2 cells, coloured fractions showed high cytotoxic effect. Total extract was most efficient to show antidiabetic effect and protective effect against various oxidative damages.	[32]
Prunus cerasus	Twig extracts from three cultivars of *Prunus cerasus*	Chemical profiling of twig extracts to determine their health-related benefits.	Compounds beneficial for health are present in twigs of tart cherry. High antioxidant, cytotoxic and antimicrobial properties were exhibited by cherry twig extracts.	[33]
Prunus avium	Ethanolic extract of stem-bark and leaf	Phytochemicals and antibacterial properties of ethanolic extracts of *Prunus avium* against some of the selected human	Biologically active compounds such as saponins, alkaloids, flavonoids, tannins and phenols were found to be present in ethanolic extract of *Prunus avium.* Antibacterial activity of the	[34]

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		pathogens: *(Staphylococcus aureus, Streptococcus pneumoniae, Escherichia coli, Enterococcus faecalis, Klebsiella pneumoniae* and *Salmonella typhi*).	extracts is due to presence of such compounds. Compared to the leaf extract, the stem-bark extract of cherry was more potent against the pathogenic bacteria.	
Prunus cornuta	Methanolic extract of bark of *Prunus cornuta* (Himalayan Bird Cherry)	Phytochemical analysis of *P. cornuta* methanolic bark extract and evaluation of their antibacterial activity that was determined by zone of inhibition in agar plates.	Steroids, terpenoids, alkaloids, tannin, saponin, proteins etc. were found in *P. cornuta* methanolic bark extract. The extract showed significant antibacterial activity against gram positive (*Staphylococcus aureus*) and gram negative (*Pseudomonas aeruginosa*) bacteria as well as fungi (*Aspergillus niger* and *Candida albicans*).	[35]
Prunus cerasus, Prunus avium, Prunus armeniaca, Prunus persica	Methanolic extract of seeds	Seeds of some of the species of *Prunus* were investigated against substantial pathogenic bacteria by zone of inhibition assay.	The highest inhibition zone diameter was obtained against *Enterococcus faecalis* in the sample of *Prunus cerasus* seeds and against *Staphylococcus aureus* in the sample of *Prunus armeniaca*. *Prunus* seed extracts may be used to develop antimicrobial agents.	[36]
Prunus avium	Alcoholic and aqueous extracts of wild cherry stem	Profile of phenolics and the antimicrobial and antioxidant properties of *Prunus avium* were evaluated.	Compared to aqueous extract, alcoholic extract exhibited higher amount of phenolics and flavonoids and showed higher ferric reduction and antioxidant property. Quercetin, catechin, chlorogenic acid and rutin were biomolecules identified in alcoholic extracts. Alcoholic extract was effective against some gram-positive bacteria such as *Staphylococcus aureus* but on other bacteria- such as gram-	[37]

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			negative *E. coli* and fungus such as *Candida albicans* the extract did not had any effect.	
Prunus avium	Fruit juice of black gold cherry (red cherry) and stark gold cherry (white cherry)	Effect of acetic acid fermentation and ethanolic fermentation on total antioxidant activity and phenolic substances of cherry was determined using oxygen radical antioxidant capacity (ORAC) and trolox equivalent antioxidant capacity (TEAC) techniques. Wine and vinegar prepared from cherry juices, were also analysed.	Red cherry juice exhibited highest phenolics and antioxidative property. Phenolics concentration and antioxidative property of white cherry juice was also very high. Macerated pulp, wine and vinegar obtained from red as well as white cherries also exhibited good phenolic content and antioxidant property. Antioxidant activity of wine samples was higher than vinegar samples.	[38]
Prunus avium	Fruit extract	Observation of physiochemical traits of fruit extract and bioactive components responsible for antioxidant capacity in sweet cherry.	Sweet cherry cultivars Mulegnana Nera and Pagliarella were found to contain highest level of phenolics, flavonoids and antioxidant property.	[39]
Prunus cerasus	Fruit extract	Determining the role of tart cherry Fruit in modulating the vascular functionality.	Significant reduction in systolic blood pressure and difference in total haemoglobin (Hb) and oxygenated Hb levels were observed post sour cherry fruit concentrate consumption.	[40]
Prunus cerasus	Fruit juice	Various properties of fruit juice were observed e.g. antioxidation property, inhibition of target enzymes in central nervous system and antidiabetic activity. The polyphenolic and anthocyanin content were quantified for determination of free radicals scavenging property of the juice.	Significant antioxidant effect was observed in sour cherry juice but the activity of lyophilised juice was not as expected. Various compounds such as ascorbic acid, gallic acid and chlorogenic acid were present in the juice. Chlorogenic acid could show inhibition against monoamine oxidase A, tyrosinase, and enzymes dysregulated in diabetes.	[41]

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Prunus avium	Methanolic and chloroform extract	The cytotoxic activity of methanolic and chloroform extracts were evaluated using Sulforhodamine-B (SRB) assay.	Both methanolic and chloroform extracts revealed potential capacity to kill cancer cells when compared with standard drugs.	[42]
Prunus avium	Seed oil extract	Using a 2, 2-diphenyl-1-picrylhydrazyl (DPPH) free radical assay, antioxidation property of various extracts and fractions were observed for *Prunus avium* seed oil.	70 percent methanolic extract ofseed oiland ethyl acetate fractions exhibited remarkable antioxidant activity.	[43]
Prunus cerasus	Seed extract	Various systemic processes, biological markers relevant to the human health were evaluated in participants after administration of seed extract of tart cherry.	Human subjects responded with an increase in value of average cell volume, mean peroxidase index, serum transferrin as well as representation of peripheral blood lymphocytes. There was a decrease in circulating neutrophil cells and ferritin level. Toxicity was not observed after consumption of tart cherry seed extract.	[44]
Prunus avium	Stem and fruit extracts	Characterisation of nutritional composition along with individual phytochemicals and bioactive components present in fruit and stem.	Higher magnitude of antioxidant property was found in stem extract compared to fruit extract whereas the antitumor potential was quite higher in fruit extract due to anthocyanins	[13]
Prunus cerasus	Fruit extract	Biological property of fruit extract of a Morello type cherry was investigated using copper catalysed human low-density-lipoprotein oxidation as experimental model.	Antioxidant and anti-glycation properties were more in fully ripened fruits compared to partially ripened fruits.	[45]
Prunus avium	Leaves methanolic extract	DNA damage protecting activity as well as the antioxidative property of Leaf extract was examined using different antioxidant	Demonstrating effective free radical scavenging activity, DNA strands of pBR322 supercoiled plasmid DNA was protected using the leaf methanolic extract in a concentration dependent manner.	[16]

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		tests: Hydrogen peroxide scavenging, (DPPH) radicals scavenging, (ABTS) radical scavenging, and metal chelating activities.		
Prunus avium	Alcoholic extract	*In vitro* sperm activation test in control group (Global media) and test group (Global media with alcoholic extract of *Prunus avium*) were analysed using the asthenozoospermic human semen samples.	Enhancing effect was seen on sperm parameters when alcoholic extract of *Prunus avium* were mixed with sperm activation media (Global media).	[15]
Prunus avium	Ethanolic extract of fruits	Different genotypes of *Prunus avium* were examined to quantify the total polyphenols as well as their antioxidant capacity using cupric ion reducing antioxidant capacity (CUPRAC) method.	Variation could be seen in polyphenolic content as well as antioxidant property of the fruit extract depending upon different genotypes. Some other factors such as ripening stage, mineral nutrition, and environmental effects had a great influence as well.	[46]
Prunus cerasus	Methanolic and aqueous extracts of fruit, root, leaf, seed, and stem-bark of tart cherry	*In vitro* screening of immunomodulatory activity of fruit, root, stem-bark, leaves and seeds using macrophages functional studies and lymphocyte proliferation assay.	Maximum potential was shown by fruit methanolic extract for NBT, iNOS and phagocytosis along with spleenocyte proliferation due to presence of bioactive compounds like flavonoids, anthocyanins etc. Whereas aqueous seed extract showed the minimum effect.	[47]
Prunus avium	Fruit extracts of Hongdeng and Rainier cultivars of *Prunus avium*	Melatonin biosynthesis, its biological role, alterations in its level that may occur during developmental stage as well as in ripened fruits.	Darkness as well as oxidative stress caused melatonin biosynthesis, leading to dual melatonin synthetic peaks during a 24-hour period. Higher temperature and higher intensity of light exposure induced upregulation of melatonin biosynthesis. Expression of tryptophan decarboxylase gene was positively correlated with melatonin	[48]

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			biosynthesis &is a rate limiting enzyme for melatonin biosynthesis in plants.	
Prunus avium and *Prunus cerasus*	Whole fruit extract, double distilled water extracted pomace and methanol extracted pomace.	Antioxidant activity and anti-inflammatory potential of the cherries were measured using a variety of versatile extraction conditions.	Anti-inflammatory compounds and antioxidant compounds are responsible for complementing each other biological effect.	[49]
Prunus cerasus	Ethyl acetate fruit extract	In vivo immunostimulatory studies of the ethyl acetate fraction obtained from sour cherry fruit and isolation of compounds from the same.	Administration of ethyl acetate fraction augmented humoral and cell mediated immune response. Increased in IgM and IgG titre, DTH reaction and enhanced cytokines (IFN-γ, IL-4, TNF-α) in BALB/c mice. Further, four molecules were isolated from this bio-fraction	[50]
Prunus cerasus	Eleven types of juice from varieties of Turkish tart cherries	Antioxidation property, total polyphenolics and the monomeric anthocyanins contents in cherry juices.	Turkish tart cherry juice exhibited excellent antioxidant potential (20.0-37.9 mmol/l TROLOX equivalents). High content of monomeric anthocyanins (350.0-633.5 mg/l) and polyphenols (1510-2550 mg/l) were reported in sour cherries. Among anthocyanins, cyanidin-3-glucosylrutinoside was present in highest concentration followed by cyanidin-3-rutinoside. Concentration of two other anthocyanins cyanidin-3-sophoroside and cyanidin-3-glucoside was found to be very low in cherry juices.	[51]
Prunus avium and *Prunus cerasus*	Cherry rootstock P HL-C (*Prunus avium* L. × *Prunus cerasus* L.)	Exploring the impact of different concentrations of Melatonin on Biochemical response and the state of morphogenesis.	1 µM melatonin resulted in increment of root length by 2.5 times and fresh weight of the root by 4 times. Due to the effect of 0.05 µM melatonin, rooting was increased by 11.11%, and 0.5 µM melatonin increased the root length. The 5 µM melatonin reduced all three	[52]

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			parameters, the number, fresh weight and rooting percentage of roots. Melatonin enhanced regeneration of roots, pigments of photosynthesis, biomass, carbohydrate and proline contents.	
Prunus cerasus, Prunus avium, Prunus microcarpa	Ethanolic fruit extract	Effect of ethanolic extract of cherry fruit on alloxan induced diabetic rats using glucometer.	The urinary microalbumin and blood glucose level were found to be reduced but an increment was observed for creatinine secretion level in urea. By controlling blood glucose level cherry extract may be used for management of diabetes.	[53]
Prunus avium	Aqueous and acetone extracts of petioles of sweet cherry.	The presence of total amount of polyphenols, flavonoids, tannins, and antioxidant capacity of extracts of dry petiole was verified among different genotypes.	The highest concentration of total polyphenols and flavonoids and highest antioxidant property was observed in the petioles of Hedelfinger sweet cherry cultivar while the lowest antioxidant activity and total polyphenol and flavonoid content was recorded in petioles of Rita cultivar. Petioles of cherry serve significant natural bioactive-phytonutrients as antioxidants.	[54]
Prunus cerasus	Fruit extract of two tart cherry cultivars, i.e. Marasca and Oblačinska	Determination of polyphenolic compounds and volatiles in fruits using HPLC and gas chromatography respectively.	Sour cherry, Marasca, has the highest level of polyphenols, chlorogenic acid, epicatechin, volatiles, flavonols, quercetin-derivatives and kaempferol. Polyphenolic compound gallocatechin was present in Marasca fruit. Hydroxycinnamic acids (HCAs), derivatives of ferulic acid, caffeic acid, p-coumaric acid and chlorogenic acid were found in both the cultivars. Concentration of chlorogenic acid was highest in Marasca. Profile of volatile compounds was similar in Marasca and Oblačinska, but total volatiles content was higher in Marasca. The principal volatile	[55]

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			substance in both the cultivars was benzaldehyde, responsible for characteristic aroma in cherry. The other important volatile compounds identified in both cultivars were hexanal, 2 - hexenal, 2 - heptanone, linalool, nerol, and α - terpineol.	
Prunus cerasus	Fruit extract	Extraction of antioxidants from fruit extract and analysis of the interaction of antioxidant capacities of various kinds of phytochemicals found in tart cherry fruit using TEAC assay and isobolographic analysis.	Strong synergistic type of interaction could be seen among compounds with highest antioxidant capacity in melatonin, kaempferol (1:2) and cyanidin 3-rutinoside and isorhamnetin 3-rutinoside (1:4). While additive or negative type of interactions could be observed for those compounds with lower antioxidant capacity.	[12]
Prunus avium	Fruit	Physicochemical properties: Total soluble solids, pH, texture, colour, juice yield, fruit mean length, width, mass, density, thickness, aspect ratio and mineral content of sweet cherry (*P. avium)* fruit were determined.	Results of physical properties were: fruit mass, 2.76 g; flesh/seed ratio, length, 17.68 mm; width, 15.60 mm; thickness, 14.89 mm; sphericity, 90.46%; aspect ratio, 88.26%; and true density, 1024.63 kg/m3.	[56]
Prunus cerasus and Prunus avium	Fruit extract	Determination of phenol content of fruits by using HPLC and antioxidant activity by using the DPPH test in two fractions, one containing flavonols, flavan-3-ols, phenolic acids and another containing anthocyanins.	Sour cherries have highest content of phenol and strong antioxidants. Contribution of anthocyanin for exerting antioxidation property was higher (~90%) than flavonols, flavan-3-ols and phenolic acids (~10%).	[57]
Prunus	Stored mature	Influences of different cytokinins during *in*	Thidiazuron was found more effective in shoot regeneration than	[58]

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avium	cotyledons	*vitro* regeneration of shoots from cotyledons of *Prunus avium*.	benzylaminopurine. Dark incubation with thidiazuron caused highest regeneration.	
Prunus serrulata var. spontanea	Methanol ethanol, acetone and aqueous extracts	Studying the comparative antioxidant activities of various solvent extracts of cherry blossom.	Methanolic extract was found to have highest phenolic content, strong DNA damage inhibition activity, and a very good radical scavenging potential. It was able to inhibit growth of human colorectal cancer cell line HT-29.	[59]
Prunus cerasus and *Prunus avium*	Fruit extract	Phenolics and anthocyanins concentration and the antineurodegenerative properties of extracts from various cultivars were analysed against neuronal cells.	Phenolics obtained from various cultivars prove to protect neural cells (PC 12) from various cellular damages caused due to oxidative stress. Being rich in phenolics, especially in anthocyanin with strong anti-neurodegenerative activity, cherries can be used as bio-functional diet.	[9]
Prunus cerasus	Fruit and callus-culture extract	Antioxidation property of fruit and callus-culture extracts were analysed using ORAC and TEAC assays.	Higher antioxidant property was detected in fruit extract compared to callus-culture extract.	[60]
Prunus cerasus and *Prunus avium*	Genomic DNA	In the S-locus in genome of sour cherry as well as sweet cherry a novel F- box protein gene was described. Blot analysis of genomic DNA was performed using probe for the F-box protein gene. RFLP bands were obtained and analysed.	The gene for F box protein showed S-haplo type specific sequence polymorphism. Expression of this gene was specific to pollens. It may be noted that the gene for F box protein are responsible for causing male determinant of gametophytic self-incompatibility in cherry plant.	[61]
Prunus avium	Fruit extract	Cherry consuming healthy women were examined for some parameters such as plasma urate, antioxidants and inflammatory markers to assess the	After consumption of sweet cherry, a decrease in plasma urate supported the antigout efficiency of cherries. Also significant decrease in inflammatory indices such as plasma C-reactive protein and nitric oxide proved the anti-inflammatory effect of the fruit.	[18]

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		physiological effects of cherry consumption.	Dehydroascorbic acid present in cherry fruits is bioavailable as vitamin C.	
Prunus cerasus	Freeze dried ground cherry, anthocyanins and cyanidin	Anti-cancerous property of cherry diet, anthocyanins and cyanidin (major anthocyanin aglycone in sour cherries) were investigated *in vivo* and *in vitro*.	Sour cherry diet, anthocyanins, and cyanidin inhibited cecal adenoma tumor development in Apc^{Min} mice and reduced proliferation of human colorectal cancer cell lines (HT 29 and HCT 116).	[62]
Prunus padus (bird cherry)	Acidified methanolic fruit extract	Quantitative analysis of anthocyanin pigments in fruits using chromatography and spectroscopy techniques.	This study revealed two types of anthocyanins in pigment composition, i.e. cyanidin-3-rutinoside and cyanidin-3-glucoside.	[63]
Prunus cerasus and *Prunus avium*	Fruit extract	Anthocyanins from sweet cherry and two cultivars of tart cherry, i.e. Balaton and Montmorency were investigated for cyclooxygenase inhibitory effect and antioxidant capacity. Extracts from the fruits of both cherries were compared to commercially available substances. The concentration of cyanidin-3-glucosylrutinoside (anthocyanin 1) and cyanidin-3-rutinoside (anthocyanin 2) were measured using HPLC.	Both the species of cherry were found to contain good amount of anthocyanins (1 as well as 2). The antioxidant property of anthocyanins from *Prunus* was almost similar to the commercially available antioxidants such as tert-butylhydroquinone, butylated-hydroxytoluene and butylated-hydroxyanisole, and superior to vitamin E. The anthocyanin content of the cherries was good enough to work as cyclooxygenase inhibitor. The cyclooxygenase inhibitory activities of anthocyanins from *Prunus* fruits were comparable to commercially available substances such as ibuprofen and naproxen.	[64]

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Prunus avium	Extracts of acids from mature and germinating seeds, seedlings and flowering trees of *Prunus avium* cultivar Stella	Qualitative determination of gibberellins in mature and germinating seeds, first-, second- and third- year seedlings and mature flowering trees was done by gas chromatography–mass spectrometry.	Different categories of gibberellins were found in mature as well as germinating seeds, young seedlings and mature flowering trees.	[65]

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Discussion

Although cherries are cultivated worldwide, low temperate regions are the most suitable habitat for cultivation. Native to Europe and southwest Asia, they are also cultivated in India's northern regions such as Jammu and Kashmir and Himachal Pradesh. Several studies have been done on cherry since ancient times, yet it still remains a matter of interest for many researchers due to their diverse varieties, unique appearance and phytochemical properties and various biological activities (in terms of effect on animals and humans), that are ever-increasing. Here we discuss different aspects of studies done over few decades, to observe the changes that took place over time. Most of the studies that have been conducted are related to phytochemical profile and biological activity of plant and their extracts prepared from different parts of plants using various solvents (aqueous and organic). Besides this, few studies are also associated with different cultivars grown, and their comparative effect on phytochemical production as well as effect of regional diversities. Cherries are single seeded drupe fruits that have varying colour according to the phytochemicals available in them[66].Although among sweet cherry varieties, Mulegnana Nera, Pagliarella, Cordia and Sylvia are known to have highest level of flavonoids and phenolics, but when compared to sour cherries, Marasca possesses higher antioxidant properties. These variations are not only limited to phytochemicals found but they may also vary from species-to-species when observed under different physiological parameters[67].Under extreme experimental conditions like high temperature and darkness, oxidative stress increases on plants. Some varieties of *Prunus avium* can combat with such harsh conditions by producing melatonin in high amount. Melatonin decreases the oxidative stress of plant to certain tolerable limits and are positively regulated by plant tryptophan decarboxylase enzyme (PaTDC), suggesting the role of this enzyme as a rate limiting factor in melatonin production. Such adaptation may not occur in all varieties of *Prunus*[48].

Among several biological properties of cherries, the most desired property is their free radical scavenging nature, which is the base for all other activities such as anti-ageing, anti-cancerous, anti-diabetic, anti-inflammatory, anti-microbial, anti-glycation, and anti-neurodegenerative properties. Research reports suggest that cherry consumption decreases inflammation, oxidative stress, muscle soreness and loss in strength and also decreases blood pressure[68].Cherries also exhibit effect on immune cells and are able to modulate the immune system[69].

Besides the physiological aspects of this plant, extensive studies have also been conducted towards phytochemicals, nutritional components, and activities as well. The major types of phytochemicals that are found in cherries are polyphenols, flavonoids, saponins, alkaloids and tannins, out of which, polyphenols and flavonoids play significant role in antioxidant activity exhibited by the fruit[3]. Although many phytochemicals play major role in enhancing medicinal properties of cherries, they are non-nutritious in nature. While sorbitol, malic acid, anthocyanin and cyanidin 3-glucosyl are some of the nutritional bioactive

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compounds found richly in its fruits[28]. As described earlier, various solvents (acidified methanol, hydro-methanol, methanol, ethyl acetate, glycerin, aqueous glycerin, chloroform, acetone, and aqueous extracts) have been used for obtaining extracts (extracts from fruits, leaves, stem, twig, bark, petiole, seed, kernel oil) to analyze the quantitative increase or decrease in concentration of bioactive compounds and the role of these compounds in different biological functioning. Mostly alcoholic extracts of different parts of plant are prepared to perform quantitative and qualitative analysis of anthocyanins, polyphenolic compounds and derivatives, and other antioxidants[23]. Most of them reduce rate of haemolysis caused due to haemoglobin oxidation. Moreover, they enhance immunomodulatory activities to prevent oxidative damage to immune system[47].

Although, plant extracts obtained with combination of chemical solvents gave fascinating results, yet simple extracts (mainly fruit extracts) also contribute much towards health benefits of animals. Anti-tumor effects against cancers such as breast and colon cancer, and prevention of cardiovascular disorders, neural disorders (anti-neurodegenerative effect), skin damage, DNA damage, increased blood glucose (anti-diabetes effect), and increased plasma urate concentration (anti-gout effect) are some of the health related properties of fruit extracts, while enhancing sperm parameters, T lymphocyte stimulation, anti-inflammatory effects are other propertiesthat contributes positively towards health of organisms[23].Other than fruit extracts, kernel oil extracts areenriched in bio-active molecules such as linoleic and oleic fatty acids, β-sitosterol, campesterol,δ (5)-avenasterol and γ-tocopherol. The stem and bark extracts may be utilized as secondary source for antioxidants, antiaging and antimicrobial compounds[20].

CONCLUSION

Various studies deciphering medicinal properties and phytochemical evaluation of cherries and their comparison have been done and some are yet to be done. The various bioactive and nutritious compounds found in cherries are flavonoids, polyphenols, anthocyanin, amino acids, vitamin C, melatonin, dietary fiber, serotonin, carotenoids, etc. Due to these phytochemicals cherries have various medicinal properties such as antioxidant, anticancer, anti-inflammatory, antiaging, and antidiabetic properties. From various studies and phytochemical comparisons of different species of cherries, it is found that sour cherry (*Prunus cerasus*) extracts have more medicinal values than sweet cherry (*Prunus avium*) extracts. Tart cherry extracts are used to treat many diseases such as arthritis, cancer, neurological disorders, retinopathy, and muscle recovery and weight management. They can be also used as a relaxant, detoxicant, astringent, antiviral, and antibacterial agents. The sweet cherry extracts also bear similar medicinal properties and are efficacious for treatment of cancer, DNA damage, gout, and inflammation.

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Over all studies suggest that every part of cherry tree is rich in essential substances required for growth, development, and maintenance of health of an organism. The non-toxic nature of cherries is the most engrossing feature, making it a delicious diet and raw material for valuable cosmetics. Thus various preparations of cherries can be either consumed or applied externally without any side effects.

Conflict of Interest

Authors declare no conflict of interest.

Acknowledgement

We would like to thank Dr. Aruna Bhatia (Professor, Punjabi University, Patiala, Punjab, India) and Dr. Qazi Parvaiz, (Senior Scientist, Indian Institute of Integrative Medicine, CSIR, J&K, India) for nurturing a scientific vision for compiling a review on "Cherries: A Treasure of Bioactive Compounds with Promising Health Promoting Functional Potential".

Funding

This review compilation work received no funding

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ISSN PRINT 2319 1775 Online 2320 7876

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