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The Blackberry: A Review on its Composition and Chemistry, Uses and Bioavailability and Potential Health Benefits

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Abstract

Garacha or Blackberry (*Rubus fruticosus* L.) is a perennial shrub that belongs to the rose family (Rosaceae). It is distributed throughout Europe, Asia, Oceania and North and South America & its fruit has medicinal, cosmetic and nutritive value. Mostly Blackberry contains anthocyanins, dietry fibers & vitamin C. The extent of each of these chemical constituents varies depending on the type of species or cultivars as well as cultivation conditions such as soil type, weather, irrigation & other horticulture practices. Blackberry is an essential component of several industrial applications that ranges from food to cosmetics to pharmaceutical products. More uses & applications of blackberry by-products are continuously added. Further research on maximizing yield per hectare and optimum preservation methods are required, especially in under-developed countries where blackberry harvesting & post-harvest methods are far traditional.

Key words: Garacha, postharvest, Rosaceae, *Rubus fruticosus*

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1. Botany

1.1. Introduction

Garacha (*Rubus fruticosus* L.) is a perennial shrub belonging to the rose family (*Rosaceae)*. It is famous for its fruit which has medicinal, nutritive and cosmetic value. The genus *Rubus is the largest genus of Rosaceae family and contains approximately 700 species*. *Rubus* consists of 12 subgenera with some domestic species [1]. *Rubus fruticosus* is distributed throughout in Europe, Oceania, North and South America and Asia. Variability prevalence is observed in morphology, flower color, growth habit & chemical composition. In this large genus, there are a lot of wild species as well as hybrids and most of them are self-infertile or dio-ecious. Therefore, such species require the cross pollination through the insects. However, cultivated species are mostly self-fertile and hermaphrodite. *Rubus fruticosus* is known by the different names depending on where we are in the world. In English is typically called, bramble or European blackberry or scald head or shrubby blackberry or Wild blackberry. In India, particularly in Hindi, it is known as Vilaayati Anchhu or kaalaa jaamun. It is known as Tût shawkî or 'Ullayq in Arabic.

Almost 400 cutivars of *Rubus fruticosus* are generated by genetic improvements [2]. The cultivars vary in firmness of fruit, shape, color, size, and weight, flavor, ripening season, yield, nutritional contents, scents and pest resistance. The most popular cultivars include Loch Ness Jumbo, Ness, Chester, Arapaho, Bartin, Navaho, Thornfree, Cacanska Bestrna, Chester Thornless, Black Satin, Dirksen Thorn less, Cherokee and 1,2, and 3 Bursa; name *Rubus fruticosus* is used before each of the cultivar name [3-4]. The plant is woody, shrubby and usually thorny except few cultivated varieties which are thornless. Its stem grows to the length of 7 m and greenish, red or purplish in color. The leaves are dark green from the upper side while light green from the underside. Seeds are light brown to dark brown and flowers are white or pale pink in color. Earlier, fruit is green, turns to red and then becomes black in color on the ripening. Blackberry has canes which are biennial and root system which is perennial. Its fresh as well as processed fruit e.g. juices, jams and jellies etc., globally represent multimillion dollar income per year on the industrial scale while interest in its medicinal properties is continuously expanding. Blackberries can be seen commonly in the gardens grown as a fruiting plant.

Over 250 compounds, the volatile compounds have been recognized in the whole blackberry fruit, juice, essence and other blackberry products. Profiles are diverse with regard to volatile compounds in blackberries which include esters, lactones, aldehydes, terpenoids, alcohols, ketones, furanone, norisoprenoids, phenolics and acids. The main active components of blackberries are phenolic compounds which are present in high amounts [5]. Because of the high phenolic amounts and high level of vitamin C, blackberry

consumption has been increased in the recent years as these compounds are used against the degenerative diseases [6-7]. Thus blackberries are those medicinal plants which are aromatic. It is obvious that blackberries vary morphologically as well as chemically due to strong influence of the environment. The source, growing conditions and the origin of plant have great impact on flavors and uses. This variability is revealed in the uses range and will be explained later in the following chapter.

1.2. History/Origin

Rubus fruticosus is believed to have origin in Armenia. Now, it is distributed all over in Europe, Oceania, North America, South America and Asia. Generic name *Rubus* is derived from Latin and its meaning is blackberry. The word *fruticosus* is also derived from a Latin word *frutico* which means shrubby or bushy. History of blackberry is steeped in legend. After Ice age, *Rubus* species were source of food and remedial or medicinal plants for the native people. Blackberries were documented in Aeschylus writings. In new world, evidence for *Rubus* species as a source of food was identified by archeologists in Newberry Crater near Bend Oregon and Hippocrates from 500 to 400 B.C.E. Egyptians of ancient times knew about blackberry, however, they did not write its uses. The first image of blackberry with description in the published form were found on *fol*. 82v–83r of Greek pharmacopeia '*Juliana Anicia Codex* or *Vindobonensis Codex'* [8]. In religious, mythological and ethnic realms, there are multiple meanings of this plant. In the Christian art, these have been represented as a symbol of spiritual ignorance. Folklore of Mediterranean says that *Rubus fruticosus* runners made the 'Christ's crown of thorns'. Blackberry deep color represents the Christ's blood. Blackberries are also considered to have an association with the omens that are bad. The stories of Europe said them the fruits of death which are tied with Wicca and are sorrow symbol. There is a legend in the Greek mythology. In that a mortal Bellerophon tried to do the riding from Pegasus to Olympus as a result of which he fell into this thorny plant, became blind and got injured. This was the punishment as he tried to take gods' power. Therefore, the blackberry fruit is also considered as a symbol of arrogance. Moreover, white wine soaked leaves and stems of blackberry as a poultice were recommended by Hippocrates for wound healing and to reduce childbirth difficulties.

1.3. Demography

Blackberry is grown in different conditions of climate and environment. However, the optimum conditions are present in cold regions. It is a hardy plant. It has the tolerance against drought and strong wind. It has ability to grow in no shade, full shade and semi-shade. For its cultivation well drained soil is preferred. Warmth, light and moisture are key requirements for cultivation of blackberry plant. Most of it is native to Europe. The genus is limited to mountain areas in the tropical and subtropical regions, however, its occurrence is not known in East Africa. The continents where blackberries are produced are Europe, North America, South America, Asia, Oceania and Africa. In Pakistan, *Rubus fruticosus* grows in Northern areas like Mansehra [9], Chitral [10], Malakand [11-12], Dir [13], and Kotli [14] *where its local names are Ach* [12], *Karwara* [10-11], *Baganrra* [15-16] and *Akhara.* Commercially, there is no cultivation of blackberry in Pakistan [9]. Statistics about the blackberry worldwide production are not available readily. However, United States and European countries are major sources of commercial crop. Average crop production is 20,000 metric tons/year in Unites States and production in Oregon is highest while it is also produced in California, Michigan, Washington, Texas, Arkansas, North Carolina, Oklahoma and Alabama but in small amounts.

According to the worldwide survey of 2005, an increase of 45% was found in production of blackberries. The survey estimated that there were 20,035 ha (hectare) for commercial crop of blackberries. Blackberries which were wild also made significant contribution in the global production as the statistics for them were 8000 ha and with 13,460 Mg (Mgagagram) harvesting. The statistics for the commercially cultivated blackberries were 7692 ha in Europe, in North America 7159 ha, in South America 1597 ha, in Central America 1640 ha, in Africa 100 ha and in Oceania 297 ha were the statistics for blackberry production. In 2005, global cultivated *Rubus fruticosus* production was 140,292 Mg [17]. The highest production of blackberries is in Europe and in North America, although, at moderate locations in Chile, South Africa, Argentina, and New Zealand, interest is increasing for their production as well as shipping to Northern markets. The main countries which produce blackberry are Iran, Asia, China, Turkey and Afghanistan. Figures about blackberry producing chief ten countries are Turkey (72,000 tons), Afghanistan (57,000 tons), China (26,000 tons), Iran (25,000 tons), United States (22,000 tons), Latvia(14,000 tons), Vietnam (12,500 tons), Bangladesh (7,000 tons), Mexico (5,700 tons), Austria (5,000 tons). The United States has the 5th place in blackberry production. The countries involved mainly in the export of blackberry are Canada (29,061 tons) and United States (6,839 tons) followed by Mexico (3,051 tons) and Rumania (4,319 tons). Further important locale for fresh blackberry import is European countries European import has doubled as compared to developing countries and is continuously increasing. In 2015, European import was 70, 000 tons. United Kingdom is the biggest importer, 52000 tons, followed by Germany 51000 tons and the Netherland 34000 tons.

1.4. Botany, Morphology, Ecology

Rubus fruticosus is a shrub whose stem is erect or trailing or arched up to the height of 7m. It is green, red or purplish in color. It is either moderately hairy or smooth. It

may be angled or rounded having several straight or curved and different sized prickles. The leaves are green in color and compound having 3 or 5 oval shaped spreading leaflets. Usually, the leaflets are dark green from upper side and light green from underside. Around the edges of leaflets, small sized teeth are present. The flowers are pink or white in color having 2 to 3 cm diameter. These are present as clusters at the ends of branches. Each flower has five petals. The fruit of blackberry changes its color as it ripens. Firstly, fruit color is green, green changes into red and red changes into black during ripening. It has 1 to 3 cm diameter. Actually the fruit is an aggregate of the fleshy drupelets and each of them contains one seed. Seed color is light brown to dark brown. Seeds are triangular to some extent. They are long about 2 to 3 mm and pitted deeply as well as irregularly. At the ground level, roots with well-defined crown are mostly present in the 20 cm of top soil but some are up to the depth of 1 m. Blackberry requires warm temperate condition. Its growth is best in the full sun and long day conditions. As the plant is hardy so it can tolerate drought. Blackberry needs the well-drained and high organic content soil. It grows best when the pH range is 6.0 to 7.0. It has short root and high demand of water.

2. Chemistry

Blackberry is a reported as a great source of phenolic compounds having antioxidant activities [18]. Blackberries have a delicious taste, nice appearance and pleasant flavor and excellent medicinal as well as nutritional value. Depending on the ecotype, blackberries have different tastes and flavors. Blackberries have varied fruit color from green to black and the plant grows to the height of 7 m. Blackberry taste is strong, citrusy and sweeter. While some others e.g. blueberries and raspberries have unique flavor. The uniqueness of fragrance in many blackberries is due to their belonging to different cultivation locale which causes changes in the blackberry chemical compounds in response to ecological conditions such as solar radiation, temperature range and soil type [6-19]. Mostly blackberries contain anthocyanins and other phenolic components, chiefly flavonols & ellagitannins, which contribute to their high antioxidant capacity. Extent of these chemical components differs depending on cultivar or species type. These are responsible for its anti-oxidant activity. Furthermore, anthocyanins give colors to different parts of plant. Other aromas come from citric acid, Furans (5-Hydroxymethylfurfural, 5-Methylfurfural, 4,5-Dimethylfurfural) and pyranone (2,3-Dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one) [20].

2.1. Chemical Composition

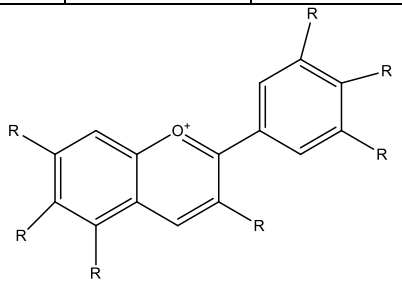
Blackberries, like other shrubby berries, also have several nutrients of plants such as minerals, dietary fibers, vitamins and anti-oxidants that are essential for best health. Blackberries possess very low fat content that is 0.5 g. Blackberries have very low level of calories that is 100 g of berries gives 43 calories. However, these are rich in insoluble as well as soluble fibers e.g. 100 g berries contain 5.3 g or 14% fiber RDA (Recommended Dietary Allowance) [21] . Blackberries have good quantity of minerals such as Calcium 41.8mg, selenium and fluoride 0.6mcg, iron 0.9mg, magnesium 28.8mg, phosphorus 31.7mg, potassium 233mg, sodium 1.4mg, zinc 0.8mg, copper 0.2mg, and manganese 0.9mg. Blackberries consist of adequate amount of vitamin A, vitamin K and vitamin E e.g. RDA per 100 g is 16%. Moderate amount of B-complex vitamins is also present in blackberries. Fresh blackberries are recommended as an excellent vitamin C (anti-oxidant) source that is RDA per100 g is 35%. Blackberries are composed of high levels of phenolic-flavonoid phytochemicals e.g. anthocyanins, salicylic acid, ellagic acid, quercetin, cyanidins, tannin, gallic acid, pelargonidins, kaempferol and catechins. Moreover, lutein, ß-carotene and zeaxanthin, the flavonoid poly phenolic antioxidants are also present in small quantity. Blackberries possess an ORAC value (Oxygen Radical Absorbance Capacity that measures the anti-oxidant strength) of about 5347µmol Trolox Equivalents/100 grams. Blackberry amounts used as food are safe, so, in medicines, it is used in large amounts.

2.2. Phyto-chemistry

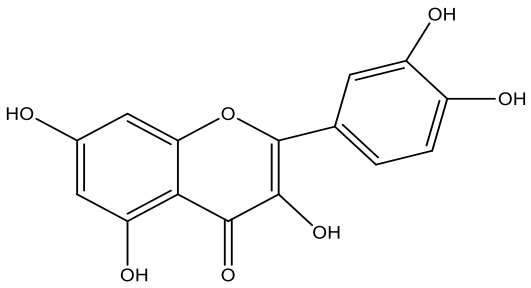
Blackberry fruit itself, and its products as well as by-products are a rich source of phytochemicals and natural antioxidants which are being explored for their health promoting activities. Various cultivars of Rubus fruticosus present different chemical composition with regard to different areas of globe. However, the plant materials usually contain following phytochemical constituents: alkaloids, flavonoids, polyphenols, tannins, anthocyanins, saponins, glycosides, terpenoids, sterols, and carbohydrate. Structures of important phytoactive constituents are shown in figure 1. Blackberries, among fruits, rank very highly for their anti-oxidant activity which is mainly because of high phenolic contents and major phenolic contents are flavanols, ellagic acid, cyanidins, ellagitannins, anthocyanins, quercetin, tannins, gallic acid and flavonols [22]. Blackberries contain the utmost level of the anthocyanins (the main anti-oxidants) which is superior to strawberry [23-24]. These flavonoids or hydrophilic color pigments give a variety of shades of blue, orange and red because of reversible variation in the structure of flavylium cation which is sensitive to intrinsic pH alteration in plant; and are present in flowers, leaves, roots, and fruits. Blackberry seed oil contains high levels of tocopherols (the vitamin E) and interesting make up of fatty acids. GCMS analysis is used for in order to find out the chemical profile of oil [25-29]. The compounds reported particularly, in seed oils of Korean thorn less blackberries were, γ-tocotrienol, α-tocopherol, δ-tocopherol and γ-tocopherol. The fatty acids present in blackberry varieties are given in Table. 1.

Table 1: Fatty acid composition and percentage in the seed oil of 2 blackberry (*Rubus fruticosus*) varieties [30]

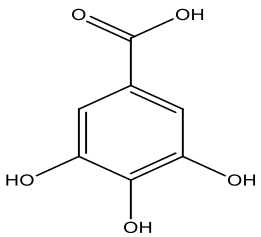
Fatty Acid	Young (R. caesius)	Boysen (R. ursinus x R. idaeus)
Palmitic acid (16:0)	2.59	3.19
Palmitoleic acid (16:1)	0.10	0.10
Stearic acid (18:0)	1.16	1.75
Oleic acid (18:1)	11.99	20.45
Linoleic acid (18:2)	51.67	57.92
Linolenic acid (18:3)	31.55	15.14
Arachidic acid (20:0)	0.37	0.68



Anthocyanin



Quercetin



Gallic acid

Figure 1. Structures of some important phytoactive constituents of *Rubus fruticosus* L.

3. Post Harvesting Technology

When harvested, berries are very perishable and maintenance of their freshness after the harvesting depends on appropriate handling and storage. The date for harvesting is decided by the surface color of berries. Usually, when more than half of the surface is colored it is harvested. Berries must be harvested close to the ripening because after harvesting, quality of eating cannot be improved. There is a legend that once, blackberries were beautiful but have to face curse by the devil Lucifer when he forced from heaven out and fell in this bush and every year on 30th September, when the berries get dark and ripened, Lucifer again enters. Generally, blackberries are harvested via hand and during the harvesting time period, these should be picked one time or two times per week. Blackberries are highly perishable so their handling must be done with extreme care. Growers pick the fruit when the temperature is low that is early morning time or at night. The marketing of blackberries should be done immediately just after picking and also after refrigeration storage at 32°F to 40°F. Generally, life of storage depends on handling of fruit during as well as after harvesting. Optimum conditions of storage (2 to 5 days) for the blackberries are 0°C temperature and relative humidity about 90-95%. Refrigeration storage causes the slowing of fruit metabolism process by lowering the temperature. Perkins *et al.* successfully perform the storage of blackberries belonging to cultivars, Navaho, Shawnee and Cheyenne, in the boxes of Plexiglas at 2ºC and under relative humidity of 95% for 7 days. There were no considerable changes soluble solids, firmness, titratable acidity and pH however, about 3.4% weight loss was also observed. To increase the shelf life, picking of berries should be avoided when they are wet, in addition, refrigerate them as soon as possible [31].

4. Processing

Because of short shelf life, fresh fruit of *Rubus fruticosus* are usually processed into dried and frozen products. These products are applied to cereal, confectionary, formulated food industry, baking, and dairy or finished into jams, canned fruit, jellies and juices to provide different blackberry market products [31]. Traditionally, for freezing, firstly blackberries are washed. If the blackberries are free of pesticides and harming chemicals, then the step of washing can be skipped and the simple need is to spread the berries on sheet of cooking. There is a wax paper on the sheet because of which berries off very quickly. Secondly, blackberries are dried completely by patting or busing a towel and then placed in the freezer. Blackberries should be completely dried before placing in freezer. For freezing 1 to 3 hours are required to freeze the berries completely. The frozen blackberries are placed in the freezer bags (made of plastic) and used for making different blackberry products. The advantage of freezing is that the amount of berries required to thaw can be taken from the bag instead of entire bag thawing. The blackberries preserved using freezer has shelf life of 10 to 12 months and these can be used for different purposes that blackberry products. Drying of blackberries is not a quick process due to juicy globes on fruit that make a waxy covering on them. When berries are boiled in water for time

of 30 s this waxy covering can be narrowed and small ruptures also occur in the outer skin of berries which facilitate in efficiently dehydrating the berries. After that he berries are dipped in the ice water to avoid their cooking and completely drained. Then picking of leaves stems and discarding of berries damaged by insects/of overripe berries is done. In the next step, the berries are evenly arranged on the trays of dehydrator leaving room between the berries for air circulation. The trays are placed in the dehydrator at 130 to 140^{o}F and dehydration is done for 10 to 18 hours till berries become leathery, tough and hard. Oven at 140^{o}F can also be used for this purpose but it takes some more hours to give dried berries. The dried berries are used to give different products.

5. Value Addition

Blackberries are rich source of nutrients and vitamins. These berries are consumed in fresh as well as processed form such as these are utilized in preparation of jams, syrups, jellies, compotes and various liqueurs. The blackberries are used as an ideal ingredient of cakes, salad of fruits, ice-cream and pastries. A variety of blackberry products are used by humans such as nectar, red wine, crushed berries along with sugar and marmalade. In the category of deserts, ice-cream with the flavor of blackberries and frozen blackberry juices (known as contesa) are also blackberry products. From the leaves of blackberry, tea is produced which helps in weight loss. Powder of blackberry fruit is used in various products that are beverages, sauces, bakery mixes as well as products of cereal, dressings, confections, and applications as natural fruit flavor/color. Natural pigments in blackberries, chiefly anthocyanins, offer attractive type colorants to manufacture jellies, dairy products, and fruit syrup. On industrial as well as domestic level, jams and jellies are produced from blackberries.

6. Uses

The blackberry fruit have medicinal, nutritional and cosmetic value. The blackberry is a rich source of important nutrients and bioactive components of remedial concern, thus, it is functionally very important food. In addition to its fresh fruit use, blackberry is also an important ingredient in salads, cooked dishes as well as in bakery goods like desserts, jams, fruit preserves and snacks. *R. fruticosus* have vitamins, tannins, minerals, steroids, acids, lipids and flavonoids that can perform different pharmacological actions such as anti-inflammatory, antioxidant, antimicrobial, anti-carcinogenic, anti-diabetic, antiviral and anti-diarrheal [32].

6.1. General Uses

Blackberries have several uses from culinary to medicine. The blackberry leaves and roots as well as root bark are used for medicinal purposes. However, for culinary use, the fruits are mainly involved. The history of blackberries is very long. European has been used blackberries for the purpose of medication for 2,000 years. According to the evidence of forensic field, Haraldskær woman from Iron Age, 2,500 years before, used the blackberries. Thus, reasonably, it can be concluded that humans have eaten blackberries more than thousands of years ago. The plant was used from Greek doctors for medicinal purposes such as diarrhea treatment or mouth disease. In folk records of medicines, it is usually impossible to identify the species used actually in past. Root of blackberry is used as decoction component for the dysentery treatment. Root has also been used for the diarrhea treatment and bush for cough treatment. Its juice has been suggested against colitis. The tea prepared from blackberry root has been consumed for the labor pain. For the tooth pain, its leaves have been chewed. The leaves have astringent effect and recommended by Pliny, Hippocrates and Dioscorides as herbal medicine. The leaves, root and bark of blackberry possess tannins in large amount which have astringent activity and thus used as herbal remedy for the treatment of digestive diseases such as gastro enteritis, diarrhea and dysentery. The blackberry leaf extract, as pleasant gargle, is used for the ulcers of mouth, mouth inflammation, throat and gum inflammation and for pain of throat [20]. Externally, the leaves of blackberry have been used for the treatment of fungal infection, eczema, rashes, injuries, acne, hemorrhoids, pain caused by stings and insect biting and oily skin. Blackberries contain high amounts of vitamin C as well as compounds of sugar, that's why, in past, these were eaten for the scurvy treatment. Anti-oxidant content is high in blackberries and therefore, to give protective result, these are used against few cancer types. The ripened blackberries possess light laxative effect due to high pectin and organic acid contents while young berries possess opposite effect due to high tannin amounts. The tannins tighten the tissues and also control the slight bleeding. Poultices are externally used on wounds as well as on bruises [21]. In the pomace of blackberries, α-tocopherol is present in high amount and has higher biological property as compared to other tocopherols which is an indication of pomace use as natural extract in pharmaceutical (anti-inflammatory, anti-oxidant), cosmetic (as α-tocopherol acetate/vitamin E in dermatology e.g. the skin creams, linoleic acid also helps in skin repairing) and food industries as an extract. Traditionally, blackberries are used to treat illnesses such as fever, bleeding, gout, discharge of vagina, colds, cystitis, flu, inflammation, cough, slow wound healing and infertility. American Indians used the stem of blackberries for the construction of strong rope.

Blackberry fruit, leaves and roots have been used several times to dye fabrics as well as hair. Nowadays, the blackberries are used fresh and also as prepared items of food e.g. desserts, yogurt, jams, wine, syrups and jellies (seedless). The flowers of blackberry are good producers of nectar which can yield fruity honey. The ripened fruits of the blackberry can be eaten uncooked or cooked and can

also be used to prepare juice, liqueurs, jams and wine. The blackberry taste is aromatic and strong. Nevertheless, it is advisable to avoid the eating of those berries which grow near busy roads because toxins from traffic gather in them.

7. Pharmacological Uses

Fruits, herbs, spices and vegetables have been consumed since long for the treatment of different human diseases in addition to their nutritive value. This potential of treatment has been credited to several bioactive and antioxidant constituents. The foremost important blackberry actions are anti-inflammatory, anti-microbial, anti-cancer and antioxidant. Various factors affect these pharmacological actions such as cultivar, ripening level, agroclimatological conditions, and method of processing. Mostly, activities are performed on the crude extracts rather than prepared standard extracts leading to non-reproducible results. Many pharmacological activities are linked with a variety of phenolics. These phenolic compounds do the scavenging of free radicals which are the main reason of pathological as well as metabolic disorders. Though several traditional medicinal uses of blackberries have been demonstrated but *in vitro* and *in vivo, both* preclinical as well as clinical work is essential for the assessment of their efficacy and safety.

7.1. Antimicrobial Activity

Usually aromatic plats showed good antimicrobial activity [33]. Riaz and his coworkers did the study of methanol extracts, extracted from different parts of blackberry plant to check its antibacterial activity against 8 strains of bacteriathat are *Salmonella typhi, Pseudomonas aeruginosa, Escherichia coli, Bacillus subtilis, Citrobacteri sp., Streptococcus aureus, Proteus mirabilis, and Micrococcus luteus*. Each of the extracts inhibited the bacterial growth. The potency order was: stem > root > leaves > fruit. [34].

7.2. Antioxidant and Anticancer Activity

Blackberries have high amounts of anthocyanins, phenols and flavonols, therefore, act as free radical inhibitors and scavengers [35]. Generally phenolic and flavonoid contents are responsible for antioxidant activity of plant [27-36]. An extract of blackberry leaves was tested and result indicated that it have high antioxidant activity that is 60.1 to 71.4 percent [37]. Thus due to this property, it showed chemo-preventive effect in the rats [38]. Antioxidant potential of blackberry was also estimated by oxygen radical absorbance capacity (ORAC) method [35]. Cyanidine-3-O-glucoside compound in the balckeberry have very strong activity as anti-oxidant thus caused the inhibition of neoplastic transformation, neoplastic cell migration as well as invasion, metastasis, activation of tumor cell markers, activation of cell migration markers and induces apoptosis in neoplastic cell (HL-60 cells) [39]. Conventional treatments against cancer such as radiotherapy, chemotherapy and surgery have side effects. Therefore, scientists are working on developing alternative remedies. Cancer cell apoptosis is a target in chemoprevention. An extract of blackberry caused apoptosis in the human leukemia HL-60 cells [40]. Further, some extracts of blackberries extracts such as Hull Thorn less, Triple Crown, and Chester Thorn less induced apoptosis in a dosage dependent mode in human leukemia cells (HL-60). This indicated that antioxidant potential leads to cancer cell apoptosis enhancement [41]. In an experiment, to check anti-cancer activity of blackberry, powder of blackberries was mixed in the diet of rats that is AIN-76 at different concentrations in the range of 5-10% and given to rats along with esophageal carcinogen N-nitrosomethylbenzylamine (NMBA) before, during and after the treatment. In 25th week, when compared with controls, all berry kinds caused the inhibition of esophageal tumors (papillomas) in the animals treated with NMBA by 24%–56%. The inhibition was found to be linked with the reduction in NMBA-induced O-6-methylguanine formation in esophageal DNA, representing that metabolism of NMBA leading to reduced DNA damage was influenced by berries and therefore, resulted in the prevention of esophageal cancer in rats [38].

7.3. Anti-Inflammatory Activity

The increasing use of blackberry fruit minimizes the inflammation risk. In vivo in the murine model, it was found as anti-inflammatory due to presence of anthocyanins. An aqueous extract of fruit water extract represented stronger activity of anti-inflammation activity even by inhibition of hyaluronidase enzyme *in vitro, f*rom the aspirin, confirming fruit's traditional anti-inflammatory use [42]. For modulation of cytokines in regulating immune or inflammatory ailments, a composition of herbs supplied with the extract of blackberry. Presence of cyanidin-3-O-glucoside in the extract of *R. fruticosus* suppresses the production of NO and thus resulted in anti- inflammatory activity [32].

7.4. Anti-diabetic Activity

R. fruticosus have anti-diabetic activity. The 70% extract of its leaves using water and butanol was found active for the non-insulin dependent diabetes treatment as well as prevention [43]. This anti-diabetic activity was tested on rats. As a result of which, the hypoglycaemic effect was observed in the normal rats and lead to conclude that it is active as counter regulatory mechanisms can't normalize the blood glucose level rapidly [44]. Chromium (Cr^{3+}) and zinc (Zn^{2+}) supplementation lessens hyperglycemia and the tea from *R. fruticosus* leaves reduced the symptoms of diabetes [45]. Practically, leaves of blackberry are suggested to control diabetes mellitus. Previously, study of blackberry anti-diabetic activity in streptozotocin (STZ)-diabetic mice, indicated anti-hyperglycaemic efficacy of *Rubus fruticosus* as a supplement of diet. In the mice, the fruit of blackberry did not affect the glucose homeostasis. Blackberry reduced the

glucose induced hyperglycemia up to 50% in alloxan diabetic rabbits by daily dosage (5g/kg of infusion) of its leaves. Ştefănuţ gave the report that when blackberry extract is administered to diabetic rats in the water of drinking for the time period of 5 weeks, a decrease in the glucose level was observed from 360 -270 mg/dL [46].

7.5. Antiviral Activity

The blackberry fruits are safe and non-toxic for human use as an antiviral agent so considered as a model candidate that can be recommended at lower expense for the human trials. It is used for the influenza treatment in combination with other medicinal plants. Its role to control the influenza virus is may be due to the polyphenol presence [47].

7.6. Neuropharmacological Activity

Riaz and coworkers evaluated different activities on mice and these activities are grouped as neuro-pharmacological activities. Methanolic extracts of *Rubus fruticosus* leaves, stem, root, and fruit were given to mice as doses of 100, 300, and 500 mg/kg. For different parts of *Rubus fruticosus*, the central nervous system depressant effect order was fruit > root > leaves > stem. All of the extracts were found to have anxiolytic nature, however, no sedative effect or relaxing activity was observed [48].

7.7. Toxicity Studies and Smooth Muscle Activities

Ali *et al.*, performed acute toxicity studies of crude methanolic extract of *Rubus fruticosus* fruits and found that LD_{50} of acute toxicity was 887.75 ± 9.22 mg/ml but CC_{50} of this extract was 13.28 ± 2.47 µg/ml in the brine shrimp. Excellent anthelmintic activity was exhibited by 20 mg/mL of extract Against *Raillientina spiralis* and *Ascaridia galli* which was 1.37 times higher than albendazole. Athough the extract is toxic but safe at 100 mg/kg. EC_{50} for spontaneous relaxant activity and for 80 mM KCl-induced contractions was 7.96 ± 0.1 and 6.45 ± 0.29 mg/ml respectively. The extract relaxed the contractions which are spontaneous in a concentration dependent mode on the jejunum preparations. The results demonstrated that smooth muscle activity was mediated through the inhibition of voltage gated channels [49].

7.8. Miscellaneous Actions and Patents

A strong action of inhibition was exhibited by the extract of blackberry on monoamino oxidase B and the concentration of inhibition that is IC_{50} was observed in the range of 4 to 7 mg/mL [50]. Both, the blackberry as well as its antioxidant compounds contribute, particularly phenolic compounds do this positively for the skin health by causing the inhibition of oxidative damage which is connected with wrinkle formation and disorders of skin like dryness of skin and hyperproliferation. Because of anti-oxidant potential and unique scent, it is useful in cosmetic industry. Blackberry is consumed frequently in preparation of skin care products, skin burns and eruptions, for facial cleansing, to treat oily skin, hair care products and acne as well as boils. Leaf extracts are used for deodorant composition and aging of skin [51]. Angiogenic properties in the aqueous extract of leaves were reported [52]. Whole plant extracts are used for prevention and cure of inflammatory, metabolic and immune diseases, as an anti-influenza medicine and also have hypoazotemic and diuretic activities. An oral medicine is prepared by using corn starch, *Gleditshcia triacanthos* powder, pectin and powdered leaves of *R. fructicosus* which is used to treat digestive disorders in piglets and calves. Toothpaste having *R. fruticosus* as active principle is used for cleaning teeth, dental caries and treating gums. For the maintenance of immune health, blackberry leaves and fruits are used normally in diet as traditional foodstuff. Powdered blackberry fruit is also a nutritional supplement [53].

7.9. Acute Toxicity

Various *Rubus fruticosus* water extract doses were administered orally to mice and lethality was checked after a, 2, 3, 4 and days. At moderate and moderate doses (0 to 6 g/kg), no significant behavioral change or death was induced by the extract in mice, but at high doses (greater than 6 g/kg), the extract caused diuresis, piloerection and fast respiration. Leaf water extract of *R. fruticosus* resulted in LD_{50}= 8.1 g/kg weight of body [44].

References

[1] M.L. Marulanda, S. Aguilar, A. Lopez. (2007). Genetic diversity of wild and cultivated *Rubus* species in Colombia using AFLP and SSR markers. Crop Breeding and Applied Technology. 7(3): 242.

[2] J. Clark, C. Finn. (2011). Blackberry breeding and genetics. Fruit, vegetable and cereal science and biotechnology. 5(1): 27-43.

[3] K.U. Yilmaz, Y. Zengin, S. Ercisli, S. Serce, K. Gunduz, M. Sengul, B.M. Asma. (2009). Some selected physico-chemical characteristics of wild and cultivated blackberry fruits (*Rubus fruticosus* L.) from Turkey. Romanian Biotechnological Letters. 14(1): 4152-4163.

[4] T. Milošević, N. Milošević, I. Glišić, J. Mladenović. (2012). Fruit quality attributes of blackberry grown under limited environmental conditions. Plant, Soil and Environment. 58: 322-327.

[5] X. DU, M. QIAN In *Flavor chemistry of small fruits: blackberry, raspberry, and blueberry*, ACS symposium series, 2010; Oxford University Press: 2010; pp 27-43.

[6] L. Ali, B. Svensson, B.W. Alsanius, M.E. Olsson. (2011). Late season harvest and storage of *Rubus* berries—major antioxidant and sugar levels. Scientia Horticulturae. 129(3): 376-381.

[7] B. Tiwari, C. O'donnell, K. Muthukumarappan, P. Cullen. (2009). Anthocyanin and colour degradation in ozone treated blackberry juice. Innovative Food Science & Emerging Technologies. 10(1): 70-75.

[8] K.E. Hummer, J. Janick In *Rubus iconography: antiquity to the Renaissance*, XXVII International Horticultural Congress-IHC2006: Global

Horticulture: Diversity and Harmony, an Introduction to IHC2006 759, 2006; 2006; pp 89-106.

[9] G.M. Shah, M.A. Khan. (2006). Common medicinal folk recipes of siran valley, Mansehra, Pakistan. Ethnobotanical Leaflets. 2006(1): 5.

[10] S. Ahmad, A. Ali, H. Beg, A.A. Dasti. (2006). OF BOONI VALLEY, DISTRICT CHITRAL PAKISTAN. Pak J. Weed Sci. Res. 12(3): 183-190.

[11] Q. Zabihullah, A. Rashid, N. Akhtar. (2006). Ethnobotanical survey in kot Manzaray Baba valley Malakand agency, Pakistan. Pak J Plant Sci. 12: 115-121.

[12] H. Sher, M.N. Alyemeni, L. Wijaya, A.J. Shah. (2010). Ethnopharmaceutically important medicinal plants and its utilization in traditional system of medicine, observation from the Northern Parts of Pakistan. Journal of Medicinal Plants Research. 4(18): 1853-1864.

[13] G. Jan, M.A. Khan, F. Gul. (2008). Ethnomedicinal plants used against diarrhea and dysentery in Dir Kohistan valley (NWFP), Pakistan. Ethnobotanical Leaflets. 2008(1): 84.

[14] M. Ajaib, Z.-u.-D. Khan, N. Khan, M. Wahab. (2010). Ethnobotanical studies on useful shrubs of district Kotli, Azad Jammu & Kashmir, Pakistan. Pak J Bot. 42(3): 1407-1415.

[15] W. Murad, A. Ahmad, S.A. Gilani, M.A. Khan. (2011). Indigenous knowledge and folk use of medicinal plants by the tribal communities of Hazar Nao Forest, Malakand District, North Pakistan. Journal of Medicinal Plants Research. 5(7): 1072-1086.

[16] H. Sher, F. Hussain. (2009). Ethnobotanical evaluation of some plant resources in Northern part of Pakistan. African Journal of biotechnology. 8(17).

[17] B.C. Strik, J.R. Clark, C.E. Finn, M.P. Bañados. (2007). Worldwide blackberry production. HortTechnology. 17(2): 205-213.

[18] G. Pantelidis, M. Vasilakakis, G. Manganaris, G. Diamantidis. (2007). Antioxidant capacity, phenol, anthocyanin and ascorbic acid contents in raspberries, blackberries, red currants, gooseberries and Cornelian cherries. Food Chemistry. 102(3): 777-783.

[19] T. Siriwoharn, R.E. Wrolstad, C.E. Finn, C.B. Pereira. (2004). Influence of cultivar, maturity, and sampling on blackberry (*Rubus* L. Hybrids) anthocyanins, polyphenolics, and antioxidant properties. Journal of Agricultural and Food Chemistry. 52(26): 8021-8030.

[20] N. Turemis, E. Kafkas, S. Kafkas, M. Kurkcuoglu, K. Baser. (2003). Determination of aroma compounds in blackberry by GC/MS analysis. Chemistry of natural compounds. 39(2): 174-176.

[21] R. Verma, T. Gangrade, R. Punasiya, C. Ghulaxe. (2014). *Rubus fruticosus* (blackberry) use as an herbal medicine. Pharmacognosy reviews. 8(16): 101.

[22] T.J. Hager, L.R. Howard, R. Liyanage, J.O. Lay, R.L. Prior. (2008). Ellagitannin composition of blackberry as determined by HPLC-ESI-MS and MALDI-TOF-MS. Journal of Agricultural and Food Chemistry. 56(3): 661-669.

[23] S.Y. Wang, H.-S. Lin. (2000). Antioxidant activity in fruits and leaves of blackberry, raspberry, and strawberry varies with cultivar and developmental stage. Journal of Agricultural and Food Chemistry. 48(2): 140-146.

[24] Ó. Acosta-Montoya, F. Vaillant, S. Cozzano, C. Mertz, A.M. Pérez, M.V. Castro. (2010). Phenolic content and antioxidant capacity of tropical highland blackberry (*Rubus adenotrichus* Schltdl.) during three edible maturity stages. Food Chemistry. 119(4): 1497-1501.

[25] A.Y. Al-Maskri, M.A. Hanif, M.Y. Al-Maskari, A.S. Abraham, J.N. Al-sabahi, O. Al-Mantheri. (2011). Essential oil from *Ocimum basilicum* (Omani Basil): a desert crop. Natural product communications. 6(10): 1934578X1100601020.

[26] Z. Arshad, M.A. Hanif, R.W.K. Qadri, M.M. Khan. (2014). Role of essential oils in plant diseases protection: a review. International Journal of Chemical and Biochemical Sciences. 6: 11-17.

[27] M.A. Hanif, M.Y. Al-Maskari, A. Al-Maskari, A. Al-Shukaili, A.Y. Al-Maskari, J.N. Al-Sabahi. (2011). Essential oil composition, antimicrobial and antioxidant activities of unexplored Omani basil. Journal of Medicinal Plants Research. 5(5): 751-757.

[28] M.A. Hanif, A.Y. Al-Maskri, Z.M.H. Al-Mahruqi, J.N. Al-Sabahi, A. Al-Azkawi, M.Y. Al-Maskari. (2011). Analytical evaluation of three wild growing Omani medicinal plants. Natural product communications. 6(10): 1934578X1100601010.

[29] I. Shahzadi, R. Nadeem, M.A. Hanif, S. Mumtaz, M.I. Jilani, S. Nisar. Chemistry and biosynthesis pathways of plant oleoresins: Important drug sources.

[30] L. Fang, W.L. Wu, H.F. Zhao, L.F. Lv, W.L. Li In *Characteristics of seed oils from four blackberries varieties (Rubus L.)*, Applied Mechanics and Materials, 2012; Trans Tech Publ: 2012; pp 273-277.

[31] R. Wu. Effects of refrigeration storage and processing technologies on the bioactive compounds and antioxidant capacities of blackberries ('Marion'and'Evergreen'). 2008.

[32] M. Zia-Ul-Haq, M. Riaz, V. De Feo, H.Z. Jaafar, M. Moga. (2014). *Rubus fruticosus* L.: constituents, biological activities and health related uses. Molecules. 19(8): 10998-11029.

[33] M.A. Hanif, H.N. Bhatti, M.S. Jamil, R.S. Anjum, A. Jamil, M.M. Khan. (2010). Antibacterial and antifungal activities of essential oils extracted from medicinal plants using CO2 supercritical fluid extraction technology. Asian Journal of Chemistry. 22(10): 7787.

[34] M. Riaz, M. Ahmad, N. Rahman. (2011). Antimicrobial screening offruit, leaves, root and

stem of *Rubus fruticosus*. Journal of Medicinal Plants Research. 5(24): 5920-5924.

[35] H. Jiao, S.Y. Wang. (2000). Correlation of antioxidant capacities to oxygen radical scavenging enzyme activities in blackberry. Journal of Agricultural and Food Chemistry. 48(11): 5672-5676.

[36] M.M. Khan, M. Iqbal, M.A. Hanif, M.S. Mahmood, S.A. Naqvi, M. Shahid, M.J. Jaskani. (2012). Antioxidant and antipathogenic activities of citrus peel oils. Journal of Essential Oil Bearing Plants. 15(6): 972-979.

[37] L. Buricova, M. Andjelkovic, A. Cermakova, Z. Reblova, O. Jurcek, E. Kolehmainen, R. Verhe, F. Kvasnicka. (2011). Antioxidant capacities and antioxidants of strawberry, blackberry and raspberry leaves.

[38] G.D. Stoner, T. Chen, L.A. Kresty, R.M. Aziz, T. Reinemann, R. Nines. (2006). Protection against esophageal cancer in rodents with lyophilized berries: potential mechanisms. Nutrition and cancer. 54(1): 33-46.

[39] M. Ding, R. Feng, S.Y. Wang, L. Bowman, Y. Lu, Y. Qian, V. Castranova, B.-H. Jiang, X. Shi. (2006). Cyanidin-3-glucoside, a natural product derived from blackberry, exhibits chemopreventive and chemotherapeutic activity. Journal of Biological Chemistry. 281(25): 17359-17368.

[40] B.L. Halvorsen, K. Holte, M.C. Myhrstad, I. Barikmo, E. Hvattum, S.F. Remberg, A.-B. Wold, K. Haffner, H. Baugerød, L.F. Andersen. (2002). A systematic screening of total antioxidants in dietary plants. The Journal of nutrition. 132(3): 461-471.

[41] S.Y. Wang, L. Bowman, M. Ding. (2008). Methyl jasmonate enhances antioxidant activity and flavonoid content in blackberries (*Rubus* sp.) and promotes antiproliferation of human cancer cells. Food Chemistry. 107(3): 1261-1269.

[42] M. Marquina, G. Corao, L. Araujo, D. Buitrago, M. Sosa. (2002). Hyaluronidase inhibitory activity from the polyphenols in the fruit of blackberry (*Rubus fruticosus* B.). Fitoterapia. 73(7): 727-729.

[43] Y. Xu, Y. Zhang, M. Chen. (2006). Effective fractions of *Rubus fruticosus* leaf, its pharmaceutical composition and uses for prevention and treatment of diabetes. China, CN1788755. 21.

[44] H. Jouad, M. Maghrani, M. Eddouks. (2002). Hypoglycaemic effect of *Rubus fructicosis* L. and *Globularia alypum* L. in normal and streptozotocin-induced diabetic rats. Journal of Ethnopharmacology. 81(3): 351-356.

[45] V. Osório e Castro. (2001). Chromium and zinc in a series of plants used in Portugal in the herbal treatment of non-insulinized diabetes. Acta Alimentaria. 30(4): 333-342.

[46] M.N. Ştefănuţ, A. Căta, R. Pop, C. Tănasie, D. Boc, I. Ienaşcu, V. Ordodi. (2013). Anti-hyperglycemic effect of bilberry, blackberry and mulberry ultrasonic extracts on diabetic rats. Plant foods for human nutrition. 68(4): 378-384.

[47] G. Corao, M. Marquina, D. Buitrago, L. Araujo, M. Sosa, Y. Buitrago. (2002). Actividad antiviral de la mora Antiviral activity of blackberries (*Rubus fruticosus* B.) mediante electroforesis en geles. Rubus fruticosus B.) gel electrophoresis. Revista Latinoamericana de Química, Rev Lat Am Quím. 30(1): 17-23.

[48] M. Riaz, M. Zia-Ul-Haq, N. Ur-Rahman, M. Ahmad. (2014). Neuropharmacological effects of methanolic extracts of *Rubus fruticosus* L. Turkish journal of medical sciences. 44(3): 454-460.

[49] N. Ali, U. Aleem, S.W.A. Shah, I. Shah, M. Junaid, G. Ahmed, W. Ali, M. Ghias. (2013). Acute toxicity, brine shrimp cytotoxicity, anthelmintic and relaxant potentials of fruits of *Rubus fruticosus* Agg. BMC complementary and alternative medicine. 13(1): 1.

[50] E. Mazzio, S. Deiab, K. Park, K. Soliman. (2013). High throughput screening to identify natural human monoamine oxidase B inhibitors. Phytotherapy Research. 27(6): 818-828.

[51] M. Herrmann, S. Grether-Beck, I. Meyer, H. Franke, H. Joppe, J. Krutmann, G. Vielhaber. (2007). Blackberry leaf extract: a multifunctional antiaging active. International Journal of Cosmetic Science. 29(5): 411-411.

[52] F.L. Greenway, Z. Liu, E.A. Woltering, Angiogenic agents from plant extracts, gallic acid, and derivatives. In Google Patents: 2010.

[53] G. Vielhaber, M. Herrmann, I. Meyer, H. Joppe, Blackberry leaf extract as an active ingredient against skin irritations and inflammations. In Google Patents: 2013.