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Research Article

Mediterranean Fruits and Berries with Bioactive and Toxic Components. A Review

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Undoubtedly, natural products with bioactive components such as fruits and berries from the Mediterranean areas are largely appreciated and highly consumed around the world due to their significance as possible novel therapeutical agents, with immense medicinal properties and a possible profound effect on health. According to epidemiological information, there were positive correlations of high consumption of fruits and berries with a low risk of various chronic diseases as these foods are rich sources of nutrients, and energy with a high content of vitamins, minerals, fiber, antioxidants, polyphenols, and numerous other classes of biological active compounds. Apart from the functional role of fruits and berries on health, they may contain components which in turn lead to toxicity on some occasions, inducing mild or severe symptoms (diarrhea, vomiting, paralysis, coma, or even death) that vary based on various factors such as dose, sensitivity of the individual and the way of exposure. Considering the above data, this paper aims to review the recent literature about the biological activities and therapeutic potentials, toxicity, and toxic components of selected Mediterranean fruits and berries, evaluating on the one hand the potential beneficial role of these foods, and on the other hand their possible toxic health effects.

Keywords: Mediterranean fruits and berries, Therapeutic bioactive components, Toxic bioactive components

Abbrevations Used: Blood glucose, BG; Burkitt's lymphoma, BL; Body Mass Index, BMI; cyclobenzaprine, CBZ; central nervous system, CNS; Glycoalkaloids, GAs; Gallic acid, GLA; Hemoglobin, HB; Hydrogen cyanide, HCN; Hydrogen cyanides, HCN; ribosome-inactivating proteins, RIP; Phenolic acids, PAs; protocatechuic acid, PCA; Phospholipase, PL; Phenothiazines, PTZ; Peptic ulcer disease, PUD; Streptozotocin, STZ; Tricyclic antidepressants, TCAs

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INTRODUCTION

The consumption and production of fruits are increasing mainly due to the potential health benefits, such as decreasing BMI and providing bioactive components as antioxidants, dietary fiber, minerals, and vitamins (Florkowski, 2019; Hurst and Hurst, 2013; Lin and Morrison, 2002; Yahia et al., 2011). In addition, consumption of at least 400 g of fruits and vegetables per day has been recommended for health promotion (WHO/FAO, 2004).

Some fruits and berries, including members of *Cucurbitaceae, Rosaceae*, and *Solanaceae*, have been used in the treatment of several diseases as essential elements of traditional medicine for centuries around the Mediterranean area (Erbay and Sari, 2018; Leporatti et al., 2003; Marc et al., 2008; Rajput, 2013). They have also been the interest of researchers as clinical treatment tools against various diseases, such as cancer and diabetes (Ahangarpour et al., 2020; Dang et al., 2017; Huseini et al., 2009).

Fruits may also contain toxic components in addition to their high phytochemical contents, such as cucurbitacins, GAs, HCN,

and RIP (Battelli et al., 1992; Dicenta, 2002; Friedman et al., 1996; Gry and Andersson, 2006; Poulton and Li, 1994). Fortunately, some of these compounds have a strong bitter taste that limits their consumption (Guil-Guerrero, 2014). In addition, they can also demonstrate beneficial effects on health (Friedman et al., 2006; Plhak et al., 1997; Kittipongpatana et al., 1999).

The toxic effects of fruits and berries can range from mild to severe symptoms (i.e., vomiting, diarrhea, paralysis, coma, death) depending on the dose, sensitivity of the individual, and the way of exposure. For instance, bloody diarrhea and acute rectorrhagia were reported upon consumption of less than 2 g of *Citrullus colocynthis* (colocynth) (Javadzadeh et al., 2013). Accidental consumptions, such as to be mistaken for non-toxic fruit, or over consumptions, such as consumption of amygdalin containing apricots have been reported to lead to toxicity (Gupta et al., 2018). In some cases, the administration of some fruits or their parts with toxic compounds to treat diseases viz. diabetes can cause hospitalization of the person (Javadzadeh et al., 2013).

Even though the consumption of fruits is crucial for good health, it may lead to toxicity on some occasions. Care should be taken against overconsumption or improper consumption. The objective of this paper is to review the biological activities and therapeutic potentials, toxicity, and toxic components of selected Mediterranean fruits mainly some of the members of Cucurbitaceae, Rosaceae, and Solanaceae families. A comprehensive review is provided focusing on *Bryonica dioica* (red bryony and white bryony) and *Citrullus colocynthis* (colocynth) from Cucurbitaceae; *Prunus armeniaca* (apricot) and *Prunus dulcis* (almond) from Rosaceae; and *Atropa belladonna* (belladonna), *Solanum dulcomara* (bittersweet), *Solanum nigrum* (black nightshade), and *Solanum linnaeanum* (devil's apple) from Solanaceae family.

1. *Atropa belladonna*

Geographic Distribution and Morphology

Atropa belladonna (belladonna or deadly nightshade) belongs to Solanaceae family and is a bushy herb having perennial growing habit. Its name belladonna is originated from the Italian word which means beautiful lady, owing to its aesthetic value and use as a facial cosmetic by women (Cikla et al., 2011). It can attain height up to 5 ft and tend to grow wildly in quarries and other marginal lands.

The plant was historically declared to be native to Europe, North Africa, and western Asia (Butcher, 1947), however it has been introduced to many countries worldwide. This plant grows vigorously in shady habitats under trees, on woodland hills, on chalk or limestones often found on rocky hillsides, steep cliffs, but retarded growth observed under direct sunny environments. *A. belladonna* is an herbaceous perennial plant characterized by purple color stem with 2–4 free branches arising near to ground. Roots are fleshy and thick, branched, white in color. Leaves are oval shaped with smooth edges and acute at apex, entire margin with short petioles, solitary, alternate phyllotaxy, one leaf of each pair larger than the other. Flowers are bell-shape and purple green in color, corolla with 5 large lobes, solitary in the axil of the leaves. Fruit are shiny black berries with five visible sepals. Seeds are small, low in germination ability, have hard seed coats and seed dormancy period (Kay, 2008).

Biological and Pharmacological Activities

A. belladonna has been used as an herbal medicine since ancient time as a pain reliever, muscle relaxer, and anti-inflammatory, and to treat menstrual problems, PUD, histaminic reaction, and motion sickness (Rajput, 2013). An extract of the plant has been used as eye drops to dilate pupils of eye pupils thus making it easier to perform eye operations and to make them look larger and thus 'more beautiful. The entire plant, harvested when coming into flower, is used to make a homeopathic remedy (Tombs and Silverman, 2004). Belladonna is used as a soothing of bronchial spasm in asthma and whooping cough, as a remedy for fever, Parkinson's disease, and pain while ointments of belladonna are applied for joint pain (rheumatism), leg pain (sciatica), and nerve pain (neuralgia). This species has an analgesic and emetic effects against miscellaneous diseases or ailments and as an antidote for snakebite (Ramoutsaki et al., 2002). Moreover, *A. belladonna* showed significant neurotropic and protective effects on behavioral and gastric alterations induced by experimental stress (Bousta, et al., 2001). The bioactivity of Belladonna could be explained by the act of its bioactive compounds as competitive antagonists at muscarinic receptors and block the binding of acetylcholine to the CNS (Berdai et al., 2012).

Toxicity to Human and Animals

Standardized Belladonna preparations are used in human phytotherapy with the maximum single dose of 0.2 g, containing 0.6 mg total alkaloids and the maximum daily dose of 0.6 g containing 1.8 mg total alkaloids (European Agency of the Evaluation Medical Products). The accidental ingestion of Belladonna in moderate doses (0.2–0.3 g) can potentially induce deadly anti-cholinergic toxidrome in humans and animals alike. However, few of hybrid plants only partially produce anticholinergic toxidrome symptoms. All anticholinergic toxidrome symptoms caused by *Atropa belladonna* poisoning are dose-dependent and consumer health status dependent (Berdai et al., 2012; Tulin and Ismet, 2011).

It is interesting to note that poisoning symptoms may manifest as over whelming higher heartbeat or tachycardia, dilatation of pupils, delirium, intensive vomiting, frequent hallucinations, occasional respiratory failure and blurring of vision. In addition, toxicity of Belladonna may also cause headaches, rashes on different body parts, urinary retention along with constipation, frequent balance loss, staggering, flushing, drying of mouth and/or throat, slurred speech, confusion, and convulsions. Furthermore, toxins absorption through the skin can potentially lead to severe skin irritation called dermatitis. In severe cases, humans or animals may become paralyzed and eventually die (Banasik and Stedeford, 2014).

The toxicity causes adverse effects on functioning of central CNS which subsequently disrupts peripheral nervous system and ultimately numerous clinical manifestations start to set in. In addition, anticholinergic syndrome exhibits a set of clinical symptoms depending upon the nature of poisoned patient. Generally, it manifests as confusions and short-term memory loss, ataxia, disorientation, hallucinations, agitated delirium, seizures, and coma. In addition, respiratory failure or cardiovascular arrest leads to death of intoxicated patient. Furthermore, adversely effected peripheral nervous system causes anticholinergic agents include mydriasis

with cycloplegia, and similar symptoms as shown by disrupted CNS. Younger children may experience speech related complexities, lethargy, and tachycardia are few of the ominous symptoms of night shade intoxication. Although, symptoms of Belladonna toxicity are quite explicit, but their precise diagnosis remains low owing to lack of physician's awareness. Even diagnosis becomes more difficult in case of indirect toxicity such as eating the meat of cattle and rabbits having been grazed on *Atropa belladonna* (Frascogna, 2007).

Moreover, nightshade intoxication related symptoms manifest as post-traumatic brain damage along with sudden and acute psychosis. Therefore, it is suggested to include unusual excitability or confusion, paralysis or coma, and related respiratory symptoms in the differential diagnosis process. However, it has been observed that exposure of patients to a drug having anticholinergic properties such as antihistamines, antispasmodics, anti-Parkinson drugs, antipsychotics, cycloplegics, CBZ, PTZ and TCAs, neuroleptics, also make it difficult to diagnose *Belladonna* toxicity. It is suggested to utilize plants having anticholinergic properties such as angel's trumpet (*Datura suaveolens*), *Salvia divinorum*, Jimsom weed (Datura Stramonium), and Black Henbane (*Hyoscyamus niger*) in differential diagnosis process to precisely diagnose *Belladonna* toxicity (Frascogna, 2007).

Toxic Components- their Chemical Structure and Localization

All plant parts contain toxic compounds. The most danger caused by berries that are attractive to children. Alkaloids are found in different plant parts in varying amounts such as roots (1.3%), leaves (1.2%), stalks (0.65%), flowers (0.6%), ripe berries (0.7%), and seeds in the range of 0.4–0.5%. Roots of *A. belladonna* reported 13 alkaloids while above ground parts of the plant revealed 7 alkaloids (Hartmann, et al., 1986). Different plant part especially leaves, and roots are rich in alkaloids including atropine, hyoscyamine and scopolamine and more abundantly; which are responsible for Anticholinergic characteristic of plants (Lee, 2007; Berdai et al., 2012; Ahmad et al., 2016).

2. *Bryonia dioica* Jacq.

Bryonia dioica Jacq. (bryony) is a climbing perennial, asparagus-like wild edible plant, member of Cucurbitaceae, and called as white bryony. It has grown and been used in several countries, such as Algeria, Bosnia-Herzegovina, Iran, Iraq, Italy, Lebanon, Morocco, Portugal, Spain, and Tunisia (Barros et al., 2011; Benarba et al., 2012; Dhouioui et al., 2016; Marc et al., 2008; Sahranavard et al., 2014; Tardío et al., 2005). The plant has been known and used for a long time, at least since the first century AD (Tardío et al., 2005). *Bryonica dioica* is one of the most commonly used elements of traditional medicine, as it has been used in treatment of arthritis, bone pains, bruises, cancer, epilepsy, infections, intestinal worms, kidney diseases, lesions, rheumatism, toothache, and wounds by the people of countries it is grown (Bahmani et al., 2015; Rafael, et al., 2011; Sahranavard et al., 2014; Touwaide et al., 2005).

Bioactivity of *B. dioica*

Main phenolic compounds of *B. dioica* were identified as luteolin 6-C-glucoside-7-O-glucoside (156 ± 15.4 mg/kg), apigenin 6-C-glucoside-7-O-glucoside (1550 ± 67.0 mg/kg), luteolin 6-C-glucoside (279 ± 3.4 mg/kg), apigenin 6-C-glucoside (318 ± 41.5 mg/kg), kaempferol 3,7-di-O-rhamnoside (82.6 ± 3 mg/kg).6, and apigenin C-hexoside-O-rhamnosyl-hexoside (24.7 ± 0.1 mg/kg) (Barros et al., 2011). Phytochemical and bioactive composition of *Bryonica dioica* was reported by several researchers (Barreira et al., 2013; García-Herrera et al., 2013; Rafael et al., 2011). Antimicrobial activity of *B. dioica* is also noteworthy that lipid extracts of roots and aerial parts of the plant demonstrated antimicrobial activity against *Escherichia coli, Salmonella typhimurium, Enterococcus faecium, Streptococcus agalactiae*, and *Staphylococcus aureus* (Dhouioui et al., 2016).

There have been several studies that encouraged the plant can be utilized in drug design against several diseases. For instance, antiproliferative activity of cucurbitacin glucosides isolated from *C. colocynthis* leaves against breast cancer was reported (Tannin-Spitz et al., 2007). Moreover, aqueous extract of *B. dioica* roots caused apoptosis in BL41 cell line and breast cancer (MDA-MB-231) cell line. In addition, aqueous extract at a concentration of 50 µg/mL also caused cell cycle arrest at G2/M phase of the breast cancer cell line (Benarba et al., 2012; Bernada et al., 2019). Furthermore, Abdessamad et al. (2019), reported that methanol extract of *B. dioica* (concentration ranged from 6.5 to 25 µg/mL) is efficient in apoptosis and inhibition of cell growth in B16F10 melanoma cancer cell line according to *in vitro* and *in vivo* tests in mice. The antitumor activity could be attributed to the induction of apoptosis via the inhibition of FAK/Src/paxillin/ERK1 expression (Abdessamad et al, 2019). On the other hand, Chekroun et al. (2016) claimed that aqueous extract of *B. dioica (20 mg/kg)* demonstrated antidiabetic activity in rats when administered intraperitoneally.

Toxicity of *B. dioica*

Scientists claimed that the toxic effects of *B. dioica* can most probably be observed on stomach and lungs. Although it has been claimed that the plant is toxic including the roots and berries (Guil-Guerrero, 2014), the number of studies reporting the cases of poisoning due to the consumption of *B. dioica* is limited. It may be due to the fact that the toxic characteristics of the plant is well-known, or it has not been used due to the bitter taste that restricts its consumption (Guil-Guerrero, 2014).

Bourhia et al. (2019) estimated the LD_{50} value of *B. dioica* extract as 500 mg/kg through oral consumption in mice. The authors also stated that aqueous extract of the plant up to a concentration of 250 mg/kg did not cause subacute toxicity in the liver and kidneys of mice.

Bryony may be toxic depending on the consumed amount. It was stated that the toxic effects could be gastrointestinal discomfort, vomiting, diarrhea, catharsis, vertigo, agitation, bradycardia, seizures, and death related to the dose (Yarnell, 2017).

3. *Citrullus colocynthis* (L.) Shrader

Citrullus colocynthis (L.) Shrader (colocynth or bitter apple or bitter cucumber or desert gourd) is a wild plant of the family *Cucurbitaceae* and mainly grown in China, Egypt, India, Iran, Jordan, Morocco, Nigeria, Pakistan, Saudi Arabia, Syria, Tunisia (Abo et al., 2008; Karim et al., 2011; Marzouk et al., 2000; Shaikh

et al., 2016). The annual or perennial plant has 4–10 cm-diameter globular fruits with ovoid seeds. In addition to its possible therapeutic uses, it can be utilized as an ornamental plant (Al-Snafi, 2015).

Citrullus colocynthis have been used in traditional medicine against asthma, bronchitis, constipation, diabetes, jaundice, joint pain, leprosy, mastitis, skin infections, and toothache. It has been used since the very early times, such as in Uygur medicine (Abo et al., 2008; Bourhia et al., 2019).

Bioactivity of *C. colocynthis*

It was suggested that extracts of leaves and roots of *C. colocynthis* can be used as alternative to synthetic pesticides, as they contain high amount of antioxidants (Ahmed et al., 2019). Moreover, it was reported that *C. colocynthis* was effective in inhibition of PLA2 activity induced by snake venom (Fatima et al., 2019).

Citrullus colocynthis has a good potential to be used in treatment of diabetes. The positive effects of daily oral administration of three 100-mg capsules containing *C. colocynthis* fruit powder, such as decreases in glycosylated HB and fasting BG levels, on patients with type II diabetes were observed in a clinical study (Huseini et al., 2009). Similar finding due to daily oral dose of 125 mg *C. colocynthis* fruit powder was also reported by Barghamdi et al. (2016).

The antidiabetic influences of *C. colocynthis* were also investigated on animal subjects. For instance, according to data of animal studies, extract of *C. colocynthis* exhibited hepatoprotective effect when orally administered to diabetic rats at a dose of 300 mg/kg for 30 d. Also, the scientific community declared that *C. colocynthis* was hepatonephroprotective and decreased plasma glucose, glycosylated Hb, and increased insulin levels in rats with diabetes, with proposed mechanism the insulin-dependent inhibition of liver gluconeogenesis, inhibition of glycogenolysis and/or insulin-insensitive enhancement of peripheral metabolism of glucose (Dallak et al., 2009).

Similarly, research data reported that the oral administration of *C. colocynthis* seed ethanol extract at a dose of equivalent to 300 mg/kg decreased BG levels and improved pancreatic and hepatic tissue of rats with alloxan-induced diabetes (Oryan et al., 2014). Hypoglycemic effect of *C. colocynthis* on test animals was also reported by researchers (Dallak et al., 2009). Oral administration of *C. colocynthis* fruit pulp powder was claimed to be effective on treatment of neuropathy due to STZ-induced diabetes in rats (Ostovar et al., 2020).

However, researchers reported that oil extract of *C. colocynthis* fruit was not effective on topical treatment of chemotherapy induced peripheral neuropathy symptoms in human according to a placebo-controlled, double-blind clinical study (Rostami et al., 2019). On the other hand, dermal absorption of *C. colocynthis* demonstrated therapeutic effects in patients with type II diabetes (Ahangarpour et al., 2020).

Anticancer activity of *Citrullus colocynthis* (L.) Shrader is also of interest, and promising results have been reported in literature. For instance, it demonstrated cytotoxic activity against breast cancer (MDA-MB-231) cell lines and colon cancer (HT-29) cell lines (Bourhia et al., 2019). Scientific community also claimed that *C. colocynthis* pulp extracts can have antiproliferative and anti-metastatic effect against MDA-MB-231 breast cancer cells (Chowdhury et al., 2017).

C. colocynthis extract attenuated colorectal cancer cell lines (WiDr, HCT-15, HCT-116) depending on the dose, and its combination with phycocyanin increased the attenuation rate as reported by a group of researchers. However, above concentrations of 2000 μg/mL of the extract and 200 μg/mL of phycocyanin were found cytotoxic against normal cells, as they caused 50% growth inhibition. The authors also stated that *C. colocynthis* extract and its combination with phycocyanin induced apoptosis by increasing the Bax and caspase-3 gene expression (Hamdan et al., 2021).

Additionally, a group of scientists claimed that *C. colocynthis* may be therapeutic in Parkinson's disease. They investigated the effects of *C. colocynthis* extracts (fruit with seeds) on mice with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced Parkinson's disease (*in vivo*) and 1-methyl-4-phenylpyridinium-induced human neuroblastoma (SH-SY5Y) cells (*in vitro*). The extracts were found protective against the symptoms of Parkinson's disease in mice and cell death due to reactive oxygen species regulated autophagy. Besides, extracts of bitter apple leaves showed analgesic activity (Yanmei et al., 2019).

Antimicrobial activity of the plant was also studied extensively. Shaikh et al. (2016) evaluated the antimicrobial activity of methanolic extract of *C. colocynthis* fruit pulp against 30 bacteria and 5 fungi species but did not observe any activity. However, Kim et al. (2014) reported that methanol extract of *C. colocynthis* fruit and its chloroform fraction exhibited antibacterial activity against *Bacillus cereus*, *Listeria monocytogenes*, *Staphylococcus aureus*, *Salmonella typhimurium*, and *Shigella sonnei*. The authors also isolated the active compound of the plant (4-methylquinoline) by chromatographic analysis and evaluated the antimicrobial activity of 4-methylquinoline analogues. They reported that 2-methyl-8-hydroxyquinoline had the highest antibacterial activity.

In another study, aqueous extracts of *C. colocynthis* seeds and pulp were utilized in production of magnetic iron oxide nanoparticles, and antimicrobial activity of the nanoparticles were reported against *Bacillus subtillis*, *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Candida albicans* (Farouk et al., 2020). Similarly, the extracts of *C. colocynthis* were used fabrication of zinc oxide nanoparticles against *B. subtilis*, *Methicillin-resistant S. aureus*, *P. aeruginosa*, and *E. coli* (Azizi et al., 2017), gold nanoparticles against *Giardia lamblia* (Al-Ardi, 2020), and silver nanoparticles against *E. coli*, *Vibrio parahaemolyticus*, *P. aeruginosa*, *Proteus vulgaris*, and *Listeria monocytogenes* (Satyavani et al, 2011). However, Satyavani et al. (2011) stated they did not observe any antimicrobial activity of the nanoparticles against *Proteus mirabilis*, *Salmonella enteritidis*, and *S. aureus*.

Toxicity of *C. colocynthis*

It should be noted that the doses of *C. colocynthis* that are even used for therapeutic purposes can have toxic effects, and the consumption of 3–4 g of the fruit can be lethal for human (De Smet, 1997). The symptoms related to *C. colocynthis* intoxication may include gastrointestinal pain, diarrhea, vomiting, diuresis, weak pulse, weakness, fainting, dizziness, fear, circulatory collapse, confusion, loss of consciousness, and death (De Smet, 1997). Reasons of exposure and toxic effects of *C. colocynthis* on humans are presented in Table 1.

TABLE 1 | Route of exposure and toxicity of *C. colocynthis* in humans.

Patient	Part of plant	Route of exposure	Toxic effect	Reference
Female (61 y)	Fruit	Accidental consumption (mistaken for zucchini)	Pseudomembranous colitis	Berrut et al., 1987
Male (34 y)	–[a]	Oral administration of unknown amount	Diarrhea, abdominal pain, dehydration	Goldfain et al., 1989
Male (37 y)	–	Oral administration of unknown amount	Diarrhea, abdominal pain, dehydration	Goldfain et al., 1989
Male (51 y)	–	Oral administration of unknown amount	Diarrhea, abdominal pain, dehydration	Goldfain et al., 1989
Female (28 y)	Dried pulp	Treatment of constipation, consumption of dried fruit (1.5 g)	Bloody diarrhea, acute rectorrhagia	Javadzadeh et al., 2013
Female (32 y)	Fruit	Treatment of type II diabetes, consumption of fresh fruit (1.6 g/d) for 2 days	Bloody diarrhea, acute rectorrhagia	Javadzadeh et al., 2013
Female (45 y)	Brewed extract	Treatment of type II diabetes, consumption of brewed extract (2 cups/d) for 2 days	Bloody diarrhea, acute rectorrhagia	Javadzadeh et al., 2013
Female (57 y)	Brewed extract	Treatment of type II diabetes, consumption of brewed extract (2 cups/d) for 4 days	Bloody diarrhea, acute rectorrhagia	Javadzadeh et al., 2013

Furthermore, the LD_{50} of extracts of immature seeds, ripe seeds, immature fruits, ripe fruits, leaves, stems, and roots of *C. colocynthis* ranged between 95.8 to 3903.2 mg/kg body mass in mice, and the leaves were the most and the stems were least toxic organs. However, the extracts at lower doses showed anti-inflammatory (1–4 mg/kg) and analgesic (0.1–8 mg/kg) activity. The LD_{50} of *C. colocynthis* seeds and roots were also reported as 385.54–2298.48 mg/kg body mass in a similar study in mice (Marzouk et al., 2011). The authors stated that the extracts (1–4 mg/kg) demonstrated good anti-inflammatory activity and estimated the LD_{50} of methanolic extract of *C. colocynthis* fruit pulp as 1000 mg/kg. They also observed alterations in histology of heart, liver, and kidneys of test animals (Shaikh et al., 2016). Doses and toxic effects of *C. colocynthis* toxicity on animals are presented in Table 2.

4. *Prunus armeniaca*

Prunus armeniaca is a member of Rosaceae family, commonly known as apricots and Armenian plum. It may be originated from Armenia where these apricots plants are wild. Soviet botanist Nikolai Vavilov has mentioned that China may be origin for this species, but according to some sources, apricots were cultivated in India around 3000 BC. *P. armeniaca* is deciduous tree prefer to grow in warm and subtropical regions up to the height of 9 to 12 meters with a trunk diameter of 35 to 40 cm. Leaves are broad and ovate with rounded base and pointed tip (Yigit et al., 2009).

March is the flowering time with white to pinkish flowers. Color of the fruits is yellow to orange; it is a drupe with single seeded with hard endocarp, soft mesocarp with glabrous exocarp. Apricot fruits generally start maturing from last week of May and continue up to August end depending upon altitude and location. Good growth of the plants can be attained when the soil pH in between 6.0 and 7.0 with well drained soils (Raj et al., 2012). Germination of seeds is very slow and need more than one year, while seeds require cold stratification for early germination. Wild plants yield nearly 47 kg per plant and fruits are used raw or cooked, and contain 6.3% of sugars, 0.7% protein, and 2.5‰ pectin. Seeds are used as raw or cooked and contains 50% of edible oil (Khalil and Rahma, 1986).

Apricot's kernel are good sources of proteins, lipids, and fatty acids in human diet. Additionally, kernel may have anti-cancer, anti-aging, anti-parasitic, anti-spasmodic, anti-mutagenic and anti-inflammatory actions, while contains various bioactive compounds as well as minerals and vitamins. After drying, apricots concentration of nutrients is increased. Oil obtained from the seeds have been used for softening of the skin (Yigit et al., 2009; Raj et al., 2012; Minaiyan et al., 2014).

Hallabo et al. (1975) reported the application of apricot oil in cosmetics and medical uses. Gezer et al. (2011) studied the physicochemical properties of Apricot kernels and observed that apricots contain crude oil (28.26% to 42.48%), crude protein, (15.7% to 18.3%) and crude fiber (5.3% to 7.1%). In addition, seeds are used in the treatment of bronchitis, cough, and constipation.

In recent years, researchers have extensively studied this plant due to its importance in commercial and medicinal applications, due to the economic and ethnomedicinal uses of *Prunus armeniaca* in Ladakh zone and observing that the dry apricots could be used for digestion, prevention of cold, cough and flu, while may contribute to lower blood pressure. Oil from the kernels is used to treat arthritis. In addition, antioxidant, and antimicrobial activities of *Prunus armeniaca* against fungal and bacterial pathogens have been assessed, with a group of investigators to report that the fruit ethanolic extract was more effective against *Staphylococcus aureus* and *Bacillus subtilis* (Abtani et al., 2008; Durmaz and Alpaslan, 2007; Yigit et al., 2009).

A group of scientists observed that apricot shows the highest antioxidant effect in both *in vitro* and *in vivo* test systems. As well as reviewed the medicinal value of apricot they stated that apricot may prevent several diseases (Gupta et al., 2018). Additionally, other researchers studied the impact of fruit and Kernel of apricot extracts on *in vitro* dissolution of cholesterol gallstones and observed that both extracts may be responsible for the dissolution of cholesterol gallstones (Tiwari and Sah, 2020).

5. *Prunus dulcis*

Prunus dulcis belongs to Rosaceae family, commonly known as Almond and native to Southwestern Asia. The plant grows naturally in Mediterranean region and is a deciduous tree growing up to 5 meters in height, and trunk up to 30 cm in diameter. Flowering take place from late January to early April. Flowers are white to pink, and fruits are 3 to 6 cm long with a thick hull. The hull consists of an endocarp with edible seed. *Prunus dulcis* nuts are traditionally consumed for its medicinal and nutritional importance (Amico et al., 2006).

Takeoka and Dao (2003) reported the antioxidant activity of *P. dulcis* fruits and the presence of biological compounds like PAs, flavonoids, tannins, and vitamins. Phytochemical characterization

TABLE 2 | Doses-dependent toxicity of *C. colocynthis* in animals.

Animal	Part of plant	Dose	Toxic effects	Reference
Chicks	Seeds	Feed, 2-10% of the basal diet for 6 w	Lesions in several organs and tissues	Bakhiet and Adam, 1995
Sheep	Fruit	Feed, 0.25 g/kg/day (*C. colocynthis* alone) and in combination with *Rhazya stricta* leaves at a dose of 0.25 g/kg/day	Toxicity with symptoms including diarrhea, weight loss, inappetence, gradual loss in condition, ataxia, recumbency, hepatic injury, death Oral administration *C. colocynthis* with *R. stricta* caused death within 26 days, 66.6% mortality	Adam et al., 2000
Rats	Fruit	Feed, 10% (*C. colocynthis* alone) and in combination with *Nerium oleander* (5% + 5%) for 6 w	Decreases in body weight gain, feed intake, and feed efficiency; diarrhea; enterohepatonephropathy; organ lesions; leucopenia, anemia Death due to the combination of *C. colocynthis* and *N. oleander*	Al-Yahya et al., 2000
Rats	Fruit	Feed, 10% (*C. colocynthis* alone) and in combination with *Cassia senna* (5% + 5%) for 6 w	Decreases in body weight and feed efficiency, diarrhea, ruffled hair, enterohepatonephrotoxicity Death due to the combination of *C. colocynthis* and *C. senna*	Adam et al., 2001
Sheep	Fruit	Oral administration, 0.25 g/kg/day (*C. colocynthis* alone for 42 d) and in combination with *N. oleander* (0.25 g/kg/day + 0.25 g/kg/day; single dose)	Diarrhea, weight loss due to administration of *C. colocynthis* alone Death due to the combination of *C. colocynthis* and *N. oleander*, mortality 100%	Adam et al., 2001
Rats	Fruit	Feed, 10% (*C. colocynthis* alone) and in combination with *Capsicum frutescens* (5%+5%) for 6 w	Decreases in body weight and feed efficiency, diarrhea, enterohepatonephrotoxicity due to *C. colocynthis* alone Death due to the combination of *C. colocynthis* and *C. frutescens*	Al-Qarawi and Adam, 2003
Rats	Alcoholic extract	Intraperitoneal administration, 50, 100, 200, 400 g/kg	Toxicity in liver	Denghani and Panjehshahin, 2006
Mice	Fruit (hydroalcoholic extract)	Treatment of pregnant mice with 30, 60, 120 mg/kg of extract for 17 d	LD_{50}:100 mg/kg Increase in mortality rate Decrease in fertility rate Decrease in number of pregnancies	Dehghani et al., 2008
Rabbit	Seeds and pulp (methanol extract)	Feed, 100 or 200 mg/kg/day	Diarrhea, anorexia due to pulp extract Death after the first dose of pulp extract at 200 mg/kg/day 50% of animals died due to pulp extract at 100 mg/kg/day Intestinal damage due to seed extract No liver or kidney damage due to seed extract No death due to seed extract	Shafaei et al., 2012
Rats	Fruit extract	Weekly oral administration of extract at a dose ¼ of LD_{50} for 10 w	LD_{50}:100, 101.7, 162.4 mg/kg (depending on where the fruit was collected from) Severe yellow diarrhea, dyspnea, depression, loss of Condition, weakness of hind limbs Toxicity in lung, liver, kidney, spleen, stomach, intestine	Elgerwi et al., 2013
Rats	Extract	40.6 mg/kg of extract on the 7th day of gestation	LD_{50}:162.4 mg/kg Teratogenesis	Elgerwi et al., 2013
Rats	Fruit (methanol extract)	Oral administration, 500, 1000, 1800, 2000, 3000 mg/kg (to determine LD_{50}); acute daily dose of 131 mg/kg	LD_{50}:1311,45 mg/kg Diarrhea, ruffled hair, acceleration of heart rate, breathing difficulty, soft feces, huddling together due to acute daily dose, change in body weight gain, hepato-nephrotoxicity	Soufane et al., 2013

of various compounds and evaluation of anti-diabetic activity of *P. dulcis* nuts have also been reported by Qureshi et al. (2016). Phytochemical composition and antiradical properties of almonds grown in Turkey was also studied (Keser et al, 2014). Chemical and Pharmacological evaluation of *Prunus dulcis* nuts (Hulls) was investigated by Qureshi et al. (2019). Impact of acute consumption of almonds on insulin sensitivity was emphasized by Jerkins et al. (2006) and Mori (2009). The lipid fraction present in almonds may be responsible for altering insulin sensitivity and promote satiety (Mori et al., 2011).

Furthermore, polyphenols which present in the almonds may have an important role in protection from chronic degenerative disorders. Indeed, consumption of almonds has been associated with reduced risk of several diseases such as hypertension, obesity, diabetes, cardiovascular diseases, and metabolic syndrome (Barreca et al., 2020). Consumption of almonds may also improve the intestinal microbiota profile and lead to health benefits. Presence of high fiber, unsaturated fat in almonds, phytochemical components and antioxidant properties may explain their protective health effects (Mori et al., 2011).

Toxic Compounds and Amygdalin in Prunus Sps (*P. dulcis* and *P. armeniaca*)

Many plants, including apricot kernel, and almonds, contain cyanogenic compounds, which have been consumed as food by human worldwide (Francisco and Pinotti, 2000). Cyanogenesis has been reported in some plants such as apricots and almonds (Seigler, 1975). Consumption of cyanogenic plants like apricot kernels and almonds has been reported to cause minor or sometimes major health hazards based on their dosage. Health problems like vomiting, headache, abdominal cramps, nausea, dizziness, convulsions, weakness, cardiac arrest, and respiratory failure have been reported (Geller et al., 2006).

Identification of allergenic proteins in almonds and its effect on various food matrices has been also reported (Tiwari et al., 2010). HCN compound was isolated from *Prunus dulcis* and named amygdalin. Amygdalin has been reported in seeds of some members of Rosaceae plants (Dicenta, 2002; Poulton and Li, 1994). In *Prunus dulcis*, bitterness was determined by the content of the cyanogenic diglucoside amygdalin. Capability of synthesizing and degrading the prunasin and amygdalin in the almond kernels has been studied (Raquel et al., 2008). Amygdalin is a glycoside, that when contact with saliva produces prussic acid or HCN, which is a poison. This is one of the nitrilosides present in some members of Rosaceae plants (Chang et al., 2006). Cyanogenic glycosides including amygdalin and taxiphyllin have been recorded in some edible fruits (Vetter, 2000). French chemists isolated the Amygdalin in 1830 and it was used for the treatment of cancer in Russia during 1845 (Dang et al., 2017).

Clinical trials were conducted by the National Cancer Institute (US) on the usage of amygdalin for the treatment of cancer but reported no evidence to support the benefits of amygdalin usage in cancer treatment though it was associated with cyanide poisoning (Milazzo and Horneber, 2015). The chemical structure of Amygdalin is D-mandelonitrile-β-D-glucoside-6-β-glucoside. Almonds and apricot consist of 100 µmol/g and 80 µmol/g amygdalin, respectively. Amygdalin is hydrolyzed by ruminal microorganisms after oral administration, and is released as glucose, benzaldehyde, and cyanide. These compounds are toxic to animals (Majak, et al., 1990; Tanyildizi, 1997). Amygdalin initially is non-toxic, but its production of HCN is poisonous and causes toxicity in animals and humans (Bolariwa et al., 2015). Berlin (1977) observed that the animal poisoning due to the cyanide-containing fruits and grasses has been a problem in cattle. There are some reports of cyanide poisoning in humans due to apricot (Gunder et al., 1969; Sayre and Kaymakcaln, 1964). Cattle, goats, and other ruminants are likely to be poisoned by species of *Prunus* due to presence of bacteria in the rumen and further speed up the process of releasing HCN from the cyanogenic glycosides. The impact of amygdalin was observed in bull reproductive system especially on motility and abnormalities of sperm cells (Tanyildizi and Bozkurt, 2004). Due to consumption of cyanogenic plants, cattle and sometimes human beings are also affected (Drochioiu et al, 2008). Scientists have investigated the potential toxic levels of apricot kernels and almond syrup. They reported that HCN levels in bitter almond (1062 ± 148.70 mg/kg) are approximately 40 times higher than levels in sweet almond (25.20 ± 8.24 mg/kg) and stated that the consumption of 50 bitter almonds is deadly for adults while 5–10 almonds are fatal for children. They also reported that apricot kernels contain 1450 mg/kg of cyanide, approximately 0.5 mg/kernel and consumers are advised to eat only five kernelsin one hour and no more than 10 per day (Chaouali et al., 2013). Finally, over consumption of apricots may cause changes in the neurotransmitter activity by acting on calcium ions (Gupta et al, 2018). In Table 3 the Toxic effects of cyanogenic foods, Prunus armeniaca and P. dulcis on humans and livestock. are presented.

TABLE 3 | Toxicity of cyanogenic foods, *Prunus armeniaca* and *P. dulcis*, in humans and livestock.

Part of the plant	Toxic effect	Reference
Consumption of cyanogenic foods like apricot kernels and almonds	Vomiting, headache, abdominal cramps, nausea, dizziness, convulsions, weakness, cardiac arrest, and respiratory failure, sometimes death	Geller et al., 2006
Consumption of almonds	Reported the allergenic proteins in almonds and its effect on various food matrices	Tiwari et al., 2010
Almonds and apricot consist of 100 µmol/g and 80 µmol/g amygdalin respectively. Amygdalin, basically is a non-toxic but its production of HCN is a poisonous and it causes toxicity in animals and human beings	Amygdalin was hydrolyzed by rumenal microorganisms after oral administration, and released as glucose, benzaldehyde, and cyanide. These compounds are toxic to animals	Majak, et al., 1990; Tanyildizi, 1997
Amygdalin (sources from almonds) basically is a non-toxic but its production of HCN is poisonous	causing toxicity in animals and human beings	Bolariwa et al., 2015
Leaves of *P. dulcis*	Animal poisoning	Berlin, 1977
Consumption of apricots	cyanide poisoning in humans	Gunder et al., 1969; Sayre and Kaymakcaln, 1964
Consumption of almonds	Impact of Amygdalin was observed in bull reproductive system especially on motility and abnormalities of sperm cells	Tanyildizi and Bozkurt, 2004
Consumption of cyanogenic Plants	cattle and sometimes human beings also affected	Drochioiu et al., 2008
Over consumption of apricots kernels and almond syrup	may cause the changes in the neurotransmitter activity by acting on calcium ions	Gupta et al., 2018

6. Members of Solanaceae Family

Solanum dulcamara L., *Solanum nigrum* L., and *Solanum linnaeanum* Hepper& P.-M.L. Jaeger., are medicinal plants belonging to the Solanaceae family and native mainly in Europe/ Mediterranean area and on other continents. These plants widely used in many traditional systems of medicine worldwide for disparate ailments but have not garnered attention for modern therapeutic uses. This could be attributed to their high alkaloid content. Alkaloids are found in all plant parts like roots, stems, leaves, flowers, fruits, and seeds. In more detail, a high content of specific alkaloids has been reported like solanine (from unripe fruits), solasodine (from flowers) and β-solamarine (from roots) (Kumar et al., 2009).

Furthermore, many chemical compounds have been identified, which are responsible for diverse activities. Many of these metabolites, like GAs, steroids and saponins, are interesting because they can have both harmful and beneficial effects on human health (Friedman et al., 2006; Plhak et al., 1997; Kittipongpatana et al., 1999). On the other hand, it should be noted that high doses of these compounds can cause gastroenteric symptoms, coma and even death. It is thought that they are toxic to human health because of their effects on the nervous system and destruction of cell membranes (Väänänen et al., 2007).

Toxicity of Solanum plants is mainly associated with the nitrates and GAs (Friedman et al., 1996), which are potentially toxic compounds that have a role in plant's protection system. The toxic dose of GAs is 2–5 mg/kg body mass, and the lethal dose is 3–6 mg/kg body mass (Alt et al., 2005; Langkilde et al., 2009; Nema et al., 2008). In *S. linnaeanum* (devil's apple) solanine seem to be more toxic than their corresponding spirosolanes, α-solamargine, α-solasonine and solasodine (Al Chami et al., 2003).

The toxic mechanism of solanine, the basic toxic compound of Solanum plants, occurs due to its interactions with the mitochondrial membrane, thereby decreasing the membrane potential and increasing the concentration of K+ in the cytoplasm, leading to apoptosis and cell damage (Gao et al., 2006). Solanine and chaconine cause neurological and gastrointestinal disorders and become lethal when the level increases more than 200 mg/kg of fresh berries and is, therefore, unsafe for human consumption. However, it should be mentioned that with a moderate use of these GAs, their ability to bind with sterols and complex cholesterol may have beneficial effects (Friedman et al., 1996; Ganguly et al., 2009).

6a. *Solanum dulcamara* L.

S. dulcamara L. (bittersweet or bittersweet nightshade or bitter nightshade), is a shrub with ivy and ascending with wooden stems, its stems are alternate green and ovoid. This European diploid species can be found from marshlands to high mountainous regions, and it is a common weed that serves as an alternative host and source of resistance genes against plant pathogens such as late blight (*Phytophthora infestans*) (Amiryousefi et al., 2018).

Plethora traditional medicinal uses of *S. dulcamara* L., have been reported in subtropical and tropical regions like Bulgaria, Italy, Iran, and Lebanon. Also, a series of pharmacological studies have been carried out to verify and validate the traditional medicinal applications of many plants in this genus. Table 4 presents *Solanum dulcamara* L. traditional medicinal uses.

The studied pharmacological activities include possible analgesic, anti-inflammatory, hypnotic, anaphrodisiac, anti-asthma rheumatism, gout (arthritis) and promotion of perspiration. *S. dulcamara* has high concentrations of GAs as degalactotigonin, atroposide E, soladulcosides A, soladulcosides B, solanine, soladulcine A, soladulcine B, 6,2′,3″,5″,4‴-pentahydroxy-3,7″-bifavone, β-sitosterol, stigmasterol, diosgenin, and inunigroside A. Table 5 presents chemical compounds from *Solanum dulcamara* L. with medicinal uses.

6b. *Solanum nigrum* L.

S. nigrum L., commonly known as makoi or black nightshade, usually grows as a weed in moist habitats in different kinds of soils, including dry, stony, shallow, or deep soils, and can be cultivated in tropical and subtropical agro-climatic regions, by sowing the seeds during April-May in well-fertilized nursery beds; it can be used for reclaiming the degraded land as well (Kiran et al., 2009).

S. nigrum L. has been used as a traditional medicinal plant to treat symptoms and diseases in many countries. In some African countries, *S. nigrum* is used as a treatment for ringworm, warts, cough, burns, dermal infections, snakebite, or stings by venomous animals. In Mauritius, used for anemia, hypotension, mouth sores. In India, reported commonly used for stomachache, stomach ulcer, wound healing. Table 6 presents *Solanum nigrum* L. traditional medicinal uses.

The previous studies have reported the presence of many bioactive compounds in *S. nigrum*, such as glycoproteins, GAs, and polyphenols, especially epicatechin, GLA, rutin, naringenin, PCA, and epicatechin, which may explain the medicinal properties of the

TABLE 4 | Traditional medicinal uses of *Solanum dulcamara* L.

Country of traditional medicine usage	Local name	Traditional medicinal indication	Parts used	Preparation	Reference
Bulgaria	Razvodnik	To promote perspiration	Aerial parts	Decoction	Leporatti et al., 2003
Italy	Dulcamara	Hypnotic, anaphrodisiac, anti-asthma	Young stems, aerial parts	Decoction	Leporatti et al., 2003
Iran	Jasmine berry, Gooseberry and Morelle douce	Analgesic remedy	Dried leaves	Decoction	Miraldi et al., 2001
Lebanon	Enab-el-dib	Rheumatism, gout (arthritis)	Whole plant	Decoction	Marc et al., 2008
Lebanon	Enab-el-dib	Rheumatism	Fruit	Decoction	Marc et al., 2008
Iran	Jasmine berry, Gooseberry and Morelle douce.	Analgesic and anti-inflammatory	Stems	Essential oil	Fallahzadeh et al., 2020

TABLE 5 | Bioactives from *Solanum dulcamara* L. with medicinal use.

Medicinal indication	Part used	Chemical compounds	Reference
Anticancer	Aerial parts	Degalactotigonin	Lee et al., 1994
Anticancer	Aerial parts	Atroposide E	Lee et al., 1994
Antiviral	Aerial parts	Soladulcosides A	Yoshida et al., 1991
Antiviral	Aerial parts	Soladulcosides B	Yoshida et al., 1991
Neurotoxicity	Stem	Solanine	Butnaru et al., 2011
Spasmolytic	Aerial parts	Soladulcine A	Lee et al., 1994
Spasmolytic	Aerial parts	Soladulcine B	Lee et al., 1994
Anticancer	Fruit	6,2′,3″,5″,4‴-Pentahydroxy-3,7″-bifavone	Sabudak, et al., 2014
Antidiabetic	Fruit	β-Sitosterol	Sabudak, et al., 2014
Antidiabetic	Fruit	Stigmasterol	Sabudak, et al., 2014

TABLE 6 | Traditional medicinal usage of *Solanum nigrum* L.

Country traditional medicine	Local name	Traditional medicinal Indication	Part used	Preparation	Reference
Somalia	Munafoqow	Against cardiac complaints	Fresh whole plant	Decoction	Samuelsson et al., 1993
Bulgaria	Tchemokutchechkogrodze	Spasmolytic, sedative	Aerial parts	Tincture	Leporatti et al., 2003
Italy	Erbamorella	Spasmolytic, sedative, antalgic, sliced fresh pulp externally applied in skin diseases, itching and painful joints	Aerial parts	Infusion	Leporatti et al., 2003
Mauritius	Brede martin	Anemia, hypotension	Leaves	Boiled	Gurib-Fakim et al., 2002
Mauritius	Brede martin	Mouth sores	Leaves	Crushed	Gurib-Fakim et al., 2002
Mauritius	Brede martin	Anemia and hypotension	Leaves	Cooked	Gurib-Fakim et al., 2002
Mauritius	Brede martin	Hypotension	Root	Decoction	Gurib-Fakim et al., 2002
Mauritius	Brede martin	Anemia	Leaves	Boiled and eaten as vegetables	Sussman et al., 1980
India	Mako	Hepatobiliary diseases	Leaves	Extract	Parveen et al., 2020
Tanzania, Africa	–	Treatment of ringworm	Leaves	Pounded and applied topically	Moshi et al., 2009
Tanzania, Africa	–	Warts	Leaves	Pounded and baked	Moshi et al., 2009
Tanzania, Africa	–	Bed wetting (for kids)	Fruit	Ripe fruits in edible form	Moshi et al., 2009
Tunisia, Africa	–	Sap	–	Erysipelas (acute Streptococcus bacterial infection)	Leporatti et al., 2009
United Republic of Congo, Africa	–	Snake bite, sting by a venomous animal	Whole plant	Maceration	Chifundera et al., 1998
Algeria, Africa	–	Blindness, conjunctivitis, glaucoma, trachoma, cataract	Fruit	Infusion	Boulos, 1983
Algeria, Africa	–	Burns	Whole plant	Decoction	Boulos, 1983
Tamil Nadu, India	–	Stomachache, stomach ulcer	Leaves	Cooked	Sivaperumal et al., 2010
Tamil Nadu, India	–	Rabies, wound healing	Leaves	Applied directly	Sivaperumal et al., 2010
Tamil Nadu, India	–	Cough	Whole plant	Applied directly	Sivaperumal et al., 2010
Himalayan region, India	–	Liver tonic, indigestion	Leaves	–	Kala et al., 2005
Thar Desert, India	–	Increase fertility in women	Root	Boiled	Parveen et al., 2007
Assam, India	–	Asthma and whooping cough	Root	Extracted juice	(Sikdar M et al., 2008)

plant. In Table 7, chemical compounds of *Solanum nigrum* L. with medicinal uses are presented.

6c. *Solanum sodomaeum* L.

Solanum linnaeanum Hepper & P.-M.L. Jaeger (devil's apple or the apple of Sodom) has long been referred as *Solanum sodomaeum* L. or *Solanum hermannii* Dunal. The latter name is illegitimate, and the former has been rejected according to the rules of botanical nomenclature and therefore not be used (Hepper and Jaeger, 1986; McNeill et al., 2012). This plant usually grows in coastal, habitats worldwide; sand dunes, grass, forest margins, riverbanks, and roadsides at 0–1200 m elevation and

TABLE 7 | Chemical compounds from *Solanum nigrum* L. with medicinal applications.

Medicinal indication	Part used	Chemical compound	Reference
Antimelanogenesis	Fruit	Diosgenin	(Suthar et al., 2008)
Antiviral	Fruit	Inunigroside A	(Ohno et al., 2012)
Leishmanicidal, antidiabetic, schistosomicidal, trypanocidal	Whole plant	Solamargine	(Ding et al., 2013)
Antibacterial, molluscicidal	Whole plant	γ-Solamargine	Ding et al., 2013
Antibacterial, molluscicidal	Whole plant	Khasianine	Ding et al., 2013
Leishmanicidal, antidiabetic, schistosomicidal	Whole plant	β1-Solasonine	Ding et al., 2013
Anticancer	Whole plant	Solasodine	Syu, et al., 2001
Antibacterial	Whole plant	Solanigroside P	Ding et al., 2013
Spasmolytic	Whole plant	Solanigroside A	Zhou et al., 2007
Spasmolytic	Whole plant	Solanigroside B	Zhou et al., 2007
Spasmolytic	Whole plant	5α-Pregn-16-en-3β-ol-20-one lycotetraoside	Zhou et al., 2007
Spasmolytic	Whole plant	Hypoglaucin H	Zhou et al., 2007
Anticancer	Leaves	Quercetin	Huang et al., 2010
Anticancer	Leaves	Rutin	Huang et al., 2010
Antidepressant, antiviral	Whole plant	Syringaresinol	Nirmal, et al., 2012
Anti-inflammatory	Whole plant	Pinoresinol	Zhao et al., 2010
Anti-inflammatory	Whole plant	Pinoresinol 4-O-β-d-glucoside	Wang, et al., 2007
Anti-inflammatory	Whole plant	Medioresinol	Zhao et al., 2010
Anti-inflammatory	Whole plant	Syringaresinol-4′-O-β-d-glucoside	Wang, et al., 2007
Antidiabetic	Leaves	Nigralanostenone	Aeri, et al., 2005
Anticancer	Whole plant	PCA	Wang, et al., 2007
Anticancer	Whole plant	Vanillic acid	Wang, et al., 2007
Anticancer	Whole plant	p-Hydroxybenzoic acid	Wang, et al., 2007
Anticancer	Leaves	3,5-Diethoxyphenol	Aeri et al., 2005
Anticancer	Whole plant	Escopoletin	Wang et al., 2007
Anticancer and antioxidant activity	Whole plant	Alpha-solanine	Shen et al., 2014
Cytotoxicity	Whole plant	Solasonine, β1-solasonine, Solamargine, β2-solamargine, Solanigroside P	Yun et al., 2014
Chemosensitizing agents	Unripen berries	Solasonine, α-solanine, Solamargine	Jagadeeshan et al., 2017
Anticancer and antioxidant activity	Berries	Polyphenols, Anthocyanins, Gas	Khan, et al., 2016
Anti-inflammatory activity	Berries	Polyphenols, Anthocyanins, Gas	Wang et al., 2017
Antileukotriene activity	Berries	Polyphenols, Anthocyanins, Gas	Cai et al., 2010
Antibacterial activity	Leaves	Solasodine	Almazini et al., 2009
Anticancer and antioxidant activity	Leaves	2,3 Dihydroxypropylelaidate; 12-sulfanyldodecanoic acid; 5-Bromosalicylaldehyde; Trilinolein; Niclofen; Usnic acid monoacetate; Naphtho [2,1-b] furan-2(1H)-one decahydro3a,6,6,9a-tetramethyl	Aboul-Eneinet et al., 2014
Transcriptional activity and cytotoxicity	Leaves	Physalin B, C, F, G, H, K Isophysalin B	Arai et al., 2014
Larvicidal activity	Mature leaves	3,7,11,15-tetramethyl-2-hexadecen-1-ol; Dodecanoic acid; 1-Hexadecanol; Benzene dicarboxylic acid; 1,2-, Dibutyl phthalate; Pregn-16-en-20-one; Sarsasapogenin 3-tosylate	Rawani et al., 2017

it is morphologically quite distinct from the rest of the eggplant wild relatives with its deeply incised, almost glabrous leaves (Weese and Bohs, 2010).

S. linnaeanum Hepper & P.-M.L. Jaeger., a plant bearing tomato-like fruit is native to southern Africa, found occasionally in many Mediterranean countries and considered a seriously invasive alien in parts of Australia and New Zealand. *S. Linnaeanum* has traditional medicinal indication in human skin tumors (anticancer), antineoplastic activity against sarcoma, anti-leukemic and gastro-intestinal ailments which are caused by *Salmonella*, *E. coli*

TABLE 8 | Traditional medicinal usage of *Solanum sodomaeum* L.

Country traditional medicine usage	Local name	Traditional medicinal indication	Part used	Preparation	Reference
Mauritius	Brinzelanguive	Reduce weight	Fruit	Cooked	Mahomoodally et al., 2018
Namibia	–	Gastro-intestinal ailments which are caused by Salmonella, E. coli and Shigella.	Roots and leaves	Extract	Iikasa et al., 2019
Australia	–	Antineoplastic activity against Sarcoma (Tumor)	Fruit	Extracted GAs.	Cham et al., 1987
Japan	–	Anti-leukaemic	Fruit	Extracted GAs.	Ono et al., 2006
Australia	–	Human skin tumors	Fruit	Extracted GAs.	Cham et al., 1987

and *Shigella* (antibacterial). Table 8 presents *Solanum sodomaeum* L. traditional medicinal uses.

CONCLUSION

In conclusion, a well-coordinated effort has been made in this review to describe a total of research data about the Mediterranean fruits and berries with bioactive compounds, focusing on either medicinal properties or therapeutic value against various diseases and supporting the valuable role of these foods on human health. However, different toxic components of selected fruits and berries from Mediterranean regions may have negative health outcomes, which in turn are probably attributed to overconsumption or improper consumption of the above products. Utilizing all the above scientific findings analyzed in this review, further research should be conducted in the future to develop new novel and therapeutic strategies against human diseases and promote the proper consumption of Mediterranean fruits and berries, reducing their toxicity cases, especially at the human level.

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CONFLICT OF INTEREST DISCLOSURE

The authors declare no conflict of interest.

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