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AN UPDATE ON PHYTOCHEMICALS, NUTRITIONAL COMPOSITION, AND PHARMACOLOGICAL SIGNIFICANCE OF *PRUNUS AMYGDALUS* BATSCH: A COMPREHENSIVE REVIEW

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ABSTRACT: *Prunus amygdalus* Batsch (family-Rosaceae), popularly known as Badam, Almond, is the most important familiar nuttree for global nut production that includes apples pears, prunes and raspberries. Almond seed skin is a prominent source of polyphenolic compounds, mainly phenolic acids, bioflavonoids, flavanones, isoflavones, flavonol glycosides and lignansthat are reported in a ripened nut. Bioflavonoids such as flavanolglycosides, chieflycatechins, epicatechin, procyanidins and flavonol include 3-hydroxyflavone backbone glycosides, particularly isorhamnetin, isorhamnetin, naringenin and kaempferol are novel agents isolated from ripened seeds. The review aims to renew the interest in this promising plant, thus stimulating researchers to go further with the study for discovering novel medicinal agents for the treatment and management of several kinds of ailments. The present study compiled a detailed and unique summary of traditional folk medicine *Prunus amygdalus* based on screening the various databases from traditional textbooks, Science Direct, Google Scholar, PubMed, Elsevier, Springer Nature, and Research Gate, *etc*. The kernels of the seeds are a major source of vitamin E and B, dietary fiber, essential elements calcium and magnesium, monounsaturated fatty acids, and phytosterols with significant cholesterol-lowering effects. It is the most popular folk remedy and nutritive food that can relieve different kinds of ailments. This review summarizes recent advances in the studies regarding *Prunus amygdalus* nutritional and therapeutic significance. Further, there is a need to isolate and evaluate the active chemical constituents of *Prunus amygdalus* having significant pharmacological values.

INTRODUCTION: A balanced diet plays a prominent role in the improvement of common health along with the management and therapy of several diseases. *Prunus amygdalus* syn. *Prunus dulcis* or *Amygdalus communis*a, traditional medicinal plant popularly known as Badam (Sweet Almond) is a member of the family Rosaceae, which has an ancient history due to its nutritional and medicinal importance.

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Moreover, seeds are rich sources of minerals and nutrients and were used as a folk medicine that manifests the utilization of this plant which cures several diseases [1, 2].

Occurrence and Distribution: The plant is indigenous to Central and Western Asia, China and Greece. Almond is indigenous to Kashmir and Punjab and is placed under the most popular crop compared to other crops of these Indian continental regions [3]. The almond is a common deciduous tree, growing at 4–10 m. The young twigs of the plant are dark green at first, but it becomes purple in contact with sunlight, and finally grey in the next year. The size of the leaves is 8–13 cm x 2.5 cm, with a serrated margin [4]. The flowers consist of five

petals with white to pale pink, arranged singly or inset and appearing before the leaves. The primary feature of the almond fruit is a drupe, a hard outer sheath that covers the ovary.

It is popularly cultivated in Mediterranean Sea regions with warm climatic conditions, summers, and mild winters. The optimal temperature required for favorable growth and development of the almonds is between 15 and 30 °C, and the tree buds have a chilling requirement of 300 to 600 hrs below 7.2 °C (45.0 °F) break the dormancy [5, 6].

Taxonomical Classification[7]:

Kingdom: Plantae

Subkingdom: Viridiplantae

Division: Tracheophyta

Subdivision: Spermatophyta

Class: Magnoliopsida

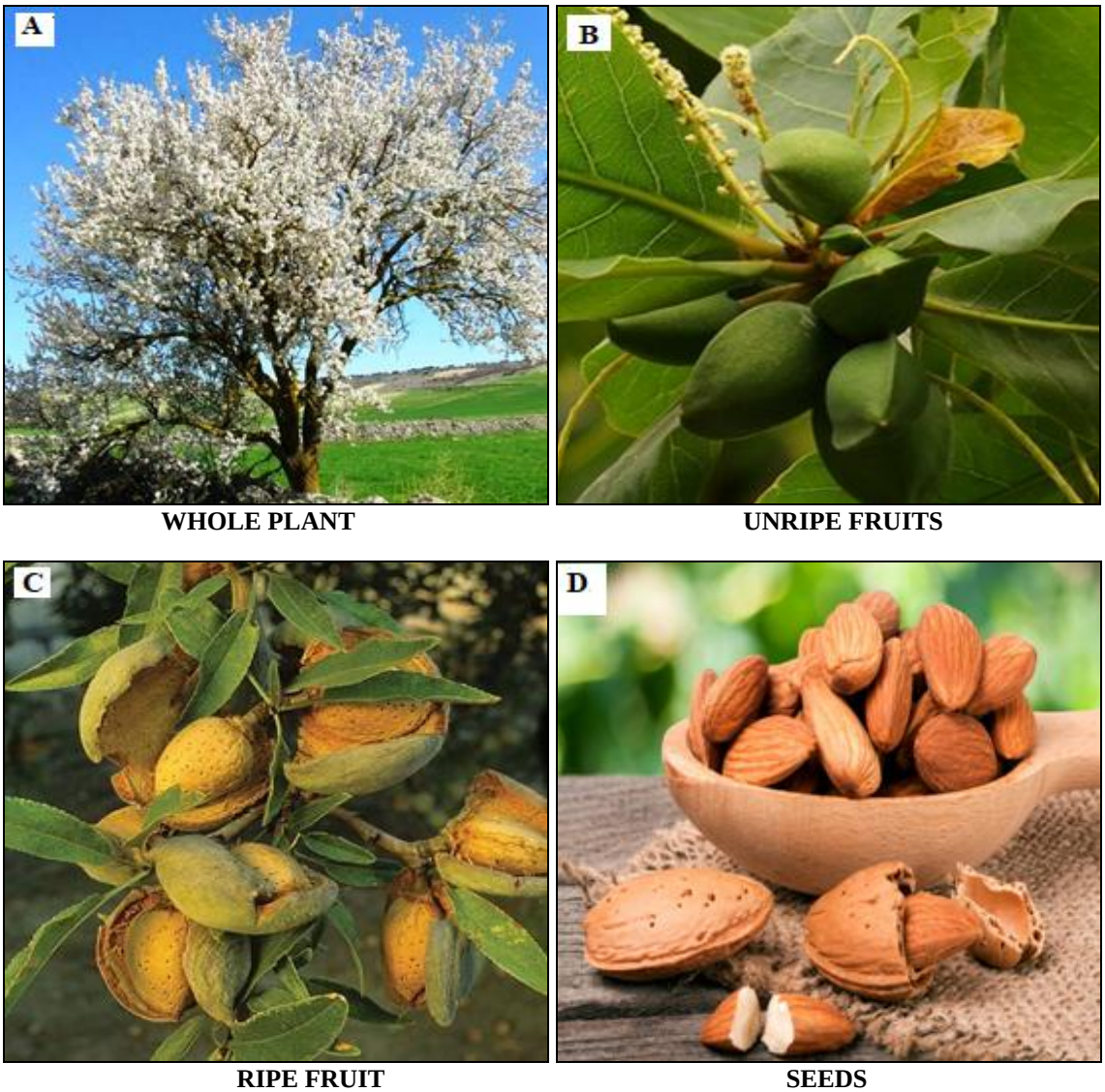
Order: Rosales

Family: Rosaceae

Genus: *Prunus*

Species: *Amygdalus*

The plant is authenticated by the taxonomic division, Banaras Hindu University (BHU), Varanasi, India, and a voucher specimen was deposited for future references (Ref. No. Rosa. 2019/1).



WHOLE PLANT **UNRIPE FRUITS**

RIPE FRUIT **SEEDS**

FIG. 1: THE WHOLE PLANT OF *PRUNUS AMYGDALUS* BATSCH ALONG WITH FRUITS COVERED BY THE HARD SEED COAT

Parts used: Entire ripened seeds and their oil, Almond shell, Fruit, and Root [8].

Literature Search: An extensive literature search was employed to summarize the traditional medicinal uses of *Prunus amygdalus* and its pharmacological properties comprising information from journals and traditional books. The literature search was carried out through search engines, namely Google Scholar and databases: PubMed, Springer, and Science Direct, and using keywords *Prunus amygdalus*, Traditional Medicine, and Pharmacological properties. The eligibility criteria of the included studies and study design were conducted according to the PICOS model (Population, Intervention, Comparison, Outcome, Study design), to report the retrieve relevant articles and to describe the data collection process in depth.

Study Design: A total of 132 articles were identified. All the irrelevant and duplicate topics or results were excluded. The complete literature search was concluded through 78 full-length manuscripts, books, and websites. No randomized controlled trials conducted on the human population were identified.

Phytochemistry: Natural products derived from plants are used for health supplements [9]. Almond seed skin has a rich source of 50−75% total phenolic content such as aldehydes and hydroxybenzoic acids, phenolic acids, flavanones, isoflavones, flavonol glycosides, flavan-3-ols, biphenyl propane derivatives, lignans, anthocyanins (cyanidin and delphinidin), procyanidins, phenolic acids and hydrolyzable tannins are isolated from the ripened nut [10, 11].

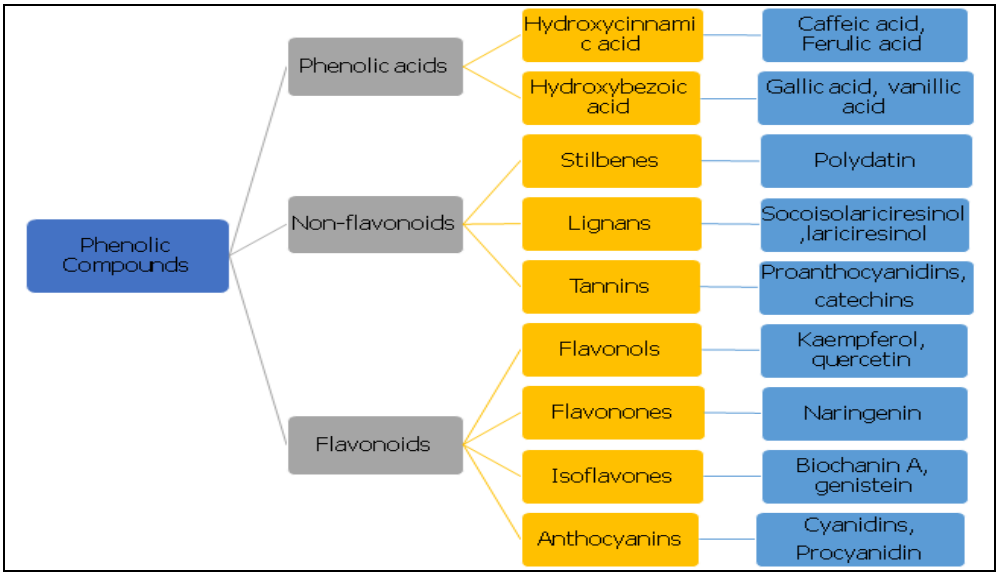


FIG. 2: CLASSIFICATION OF PHENOLIC COMPOUNDS ISOLATED FROM *PRUNUS AMYGDALUS* BATSCH

Commonly bioflavonoids such as flavanol include catechins epicatechin and procyanidins, and flavonol includes 3-hydroxyflavone backbone glycosides, particularly isorhamnetin-3-O-glucoside, isorhamnetin-3-O-rutinoside, naringenin-7-O-glucoside and kaempferol-3- O-rutinoside are the chief bioactive of ripened seeds[12, 13, 14] by kernel bitterness. The taste of the bitter almond is due to the presence of cyanogenic glycosides in its kernel known as amygdalin **Fig. 3B** and prunasin **Fig. 3C,** whereas both chemical constituents are absent in sweet almonds [15, 16]. Prunasin is an important cyanogenetic monoglycoside, isolated from unripe almonds seeds, and after ripening, it is converted into cyanogenetic diglycoside known as amygdalin. Sweet almond oil is placed under unsaturated oil consisting of oleic acid as a chief fatty acid [17], with a little amount of β-sitosterol **Fig. 3D** and α-tocopherol **Fig. 3N** [18, 19]. Quality control analysis by HPLC techniques, polyphenolic compounds such as Gallic acid, Ellagic acid, caffeic acid **Fig. 3E**, ferulic acid **Fig. 3F**, p-coumaric acid, Vanillic acid **Fig. 3G** (After basic hydrolysis) and kaempferol **Fig. 3H**, catechin **Fig. 3I**, epicatechin, isorhamnetin **Fig. 3J,** and quercetin **Fig. 3O**, delphinidin and cyanidin along with an important compounds procyanidins B2 and B3 **Fig. 3A** were

isolated from the almond seed [20]. In another study, researchers have isolated a new phenolic compound from almond skins known as quercetin, kaempferol, naringenin **Fig. 3K** conjugated to sugar moiety glucose galactose, or rhamnose, along with catechin, protocatechuic acid, vanillic acid, and benzoic acid [21]. The detailed structural presentation of major bioactive is mentioned in **Fig. 3** and their contents in different parts kernel, skin, shell, and hull are reported in **Table 1.**

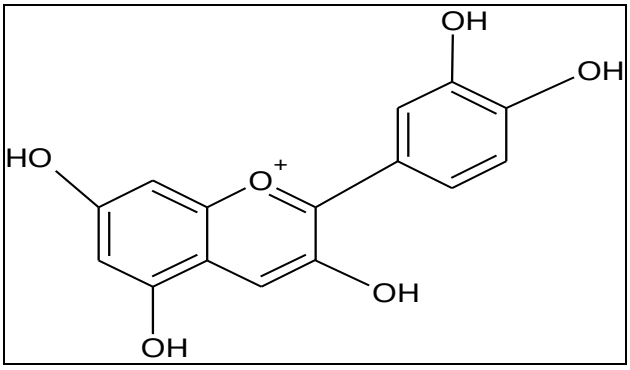


FIG. 3A: PROCYANIDINS

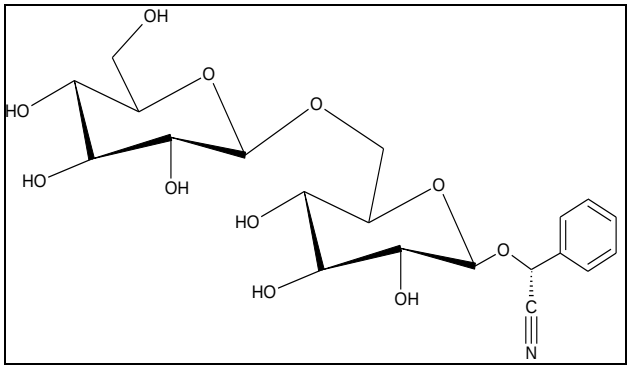


FIG. 3B: AMYGDALIN

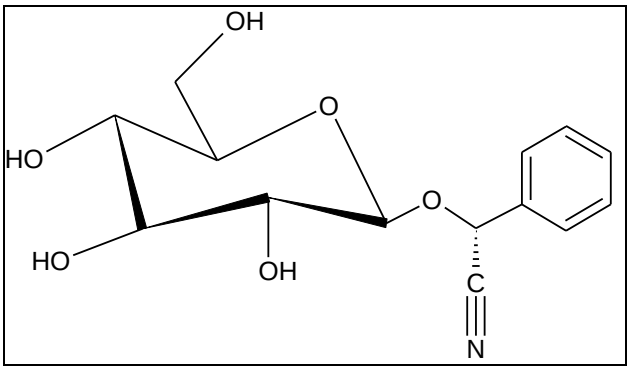


FIG. 3C: PRUNASIN

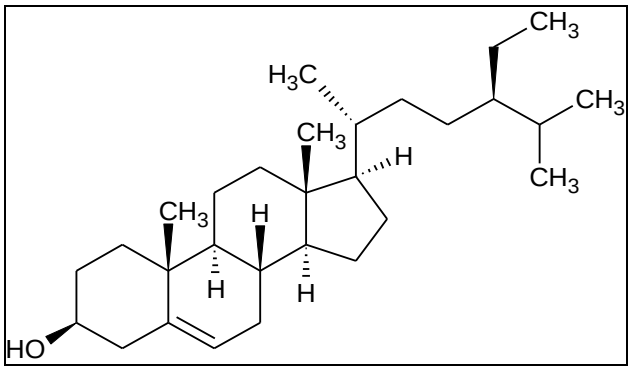


FIG. 3D: β-SITOSTEROL

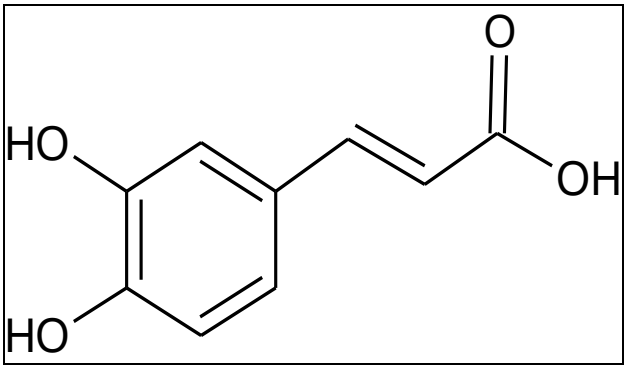


FIG. 3E: CAFFEIC ACID

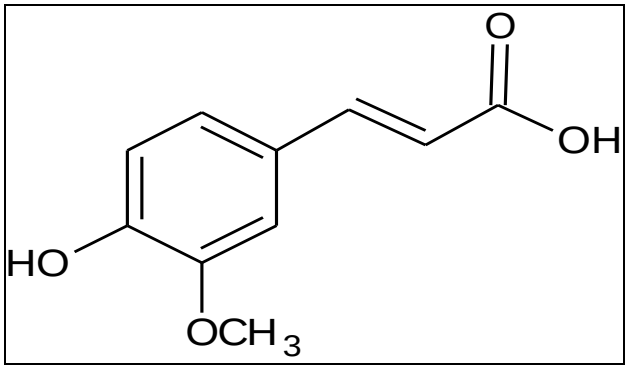


FIG. 3F: FERULIC ACID

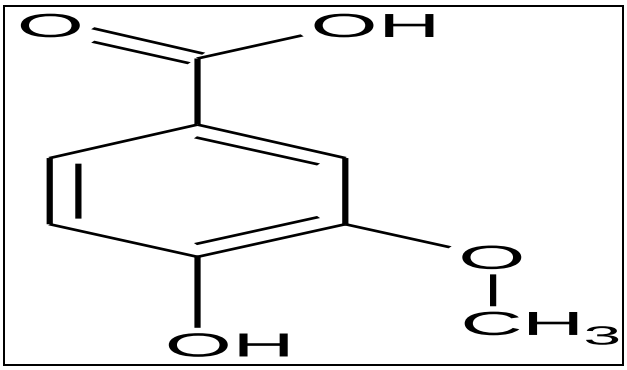


FIG. 3G: VANILLIC ACID

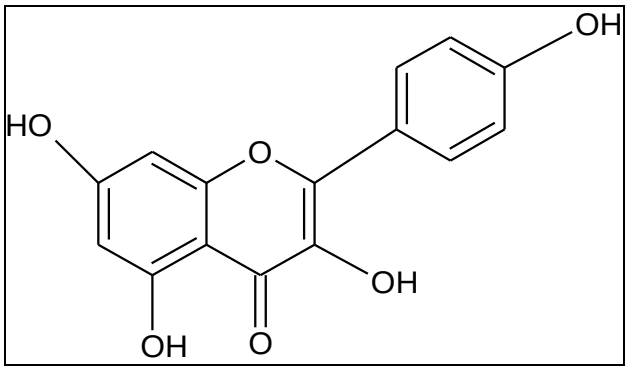


FIG. 3H: KAEMPFEROL

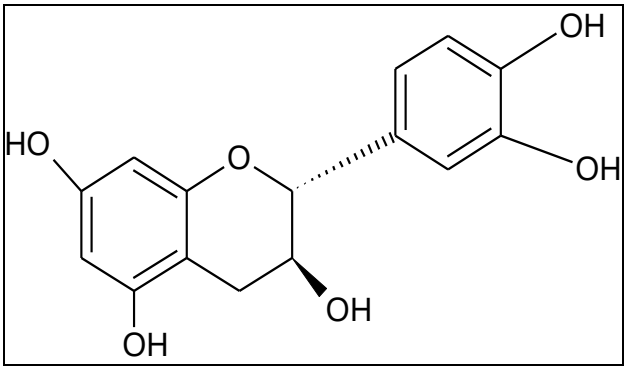


FIG. 3I: CATECHIN

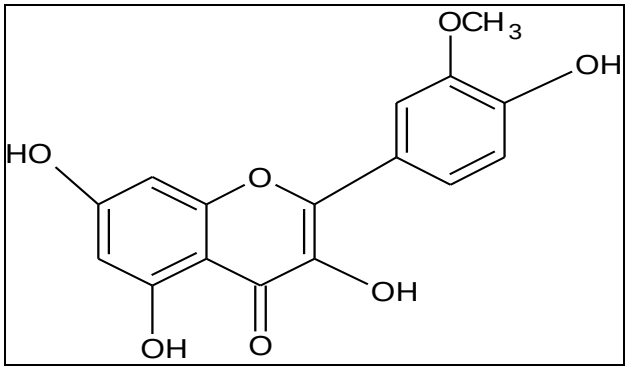


FIG. 3J: ISORHAMNETIN

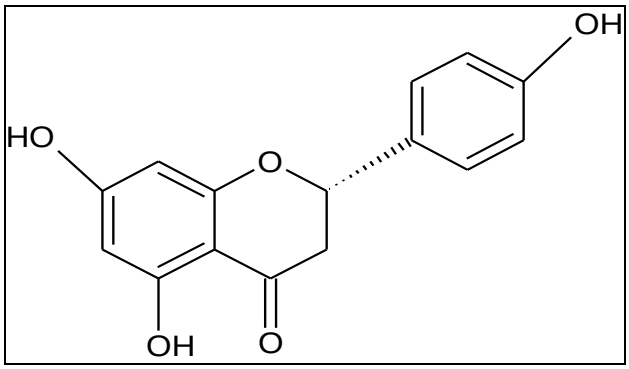


FIG. 3K: NARINGENIN

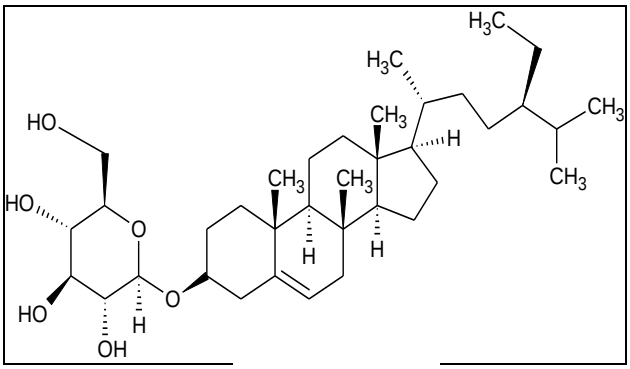


FIG. 3L: DAUCOSTEROL

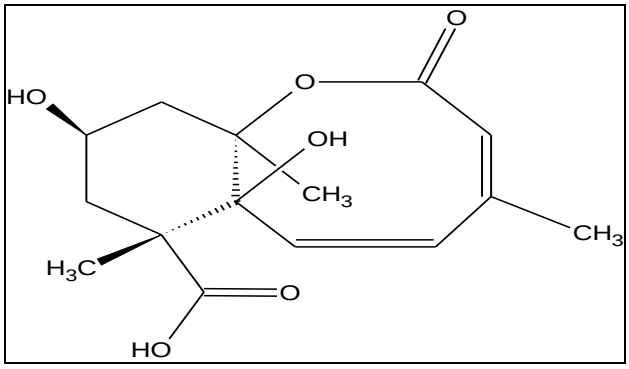


FIG. 3M: AMYGDALACTONE

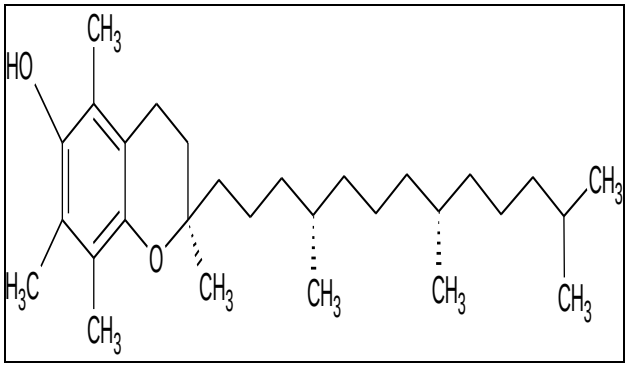


FIG. 3N: *α*-TOCOPHEROL

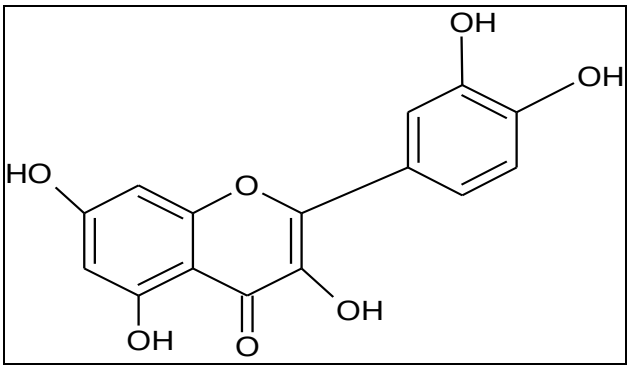


FIG. 3O: QUERCETIN

FIG. 3: LIST OF CHEMICAL STRUCTURES OF CHIEF BIOACTIVE REPORTED IN *PRUNUS AMYGDALUS*

Researchers have isolated nine new polyphenolic natural products from the ethyl acetate and n-butanol fraction of *Prunus amygdalus* seed skin. As per characterization by NMR, Mass spectra and compared with the literature survey, the following phytoconstituents were identified as 3b-O-methylquercetin 3-O-a-D-glucopyranoside, 3b-O-methylquercetin 3-Oa- D-galactopyranoside, 3b-O-methylquercetin 3-O-R-Lrhamnopyranosyl-(1-6)-a-D-glucopyranoside, kaempferol 3-O-R-L-

rhamnopyranosyl - (1 - 6) – a - D-glucopyranoside, naringenin 7-O-a-D-glucopyranoside, catechin, protocatechuic acid, vanillic acid and p-hydroxybenzoic acid [22]. Another study isolated sesquiterpene lactone derivatives are known as amygdalactone **Fig. 3M** from the hulls of *Prunus amygdalus* [23].

New study researchers have isolated another active agent such as 1-O-beta-D-glucopyranosyl - (2S, 3R, 4E, 8Z) – 2 - [(2R) - 2-hydroxyhexadecanoylamino] - 4, 8-octadecadiene-1, 3-diol, sphingolipid, β -sitosterol, daucosterol **Fig. 3I**, uridine and adenosine, from the nuts of *Prunus amygdalus* [24].

TABLE 1: BIOACTIVE CONTENTS IN DIFFERENT PARTS OF THE *PRUNUS AMYGDALUS*

Type of Secondary metabolites	Name of Phytoconstituents	Content				Ref.
		Kernel	Skin	Shell	Hull	
Hydroxybenzoic acids	p-Hydroxybenzoic acid	–	+	–	–	22
	Vanillic acid	–	+	–	–	22
	Protocatechuic acid	+	+	–	–	66; 67
Hydroxycinnamic acids	Ferulic acid	Trace	2.19 ± 0.01	–	2.71 ± 0.02	68
	Sinapic acid	Trace	9.51 ± 0.03 µg/g	–	9.92 ± 0.02	68
	Caffeic acid	Trace	Trace	–	Trace	68
	Chlorogenic acid	–	10.6–3.12 µg/g	–	–	66
Anthocyanidin and procyanidin	Delphinidin	+	–	–	–	69
	Cyanidin	+	–	–	–	69
	(-)-Epicatechin	–	+	–	–	66
	Procyanidin B3 + B1	–	+	–	–	66
	Procyanidin B2	+	–	–	–	69
Flavonol glycosides	Kaempferol-3-O-rutinoside	+	+	–	–	67
	Kaempferol-3-O-glucoside	–	1.65 µg/g	–	–	22, 66
	Isorhamnetin-3-O-rutinoside	–	27.6–41.4 µg/g	–	–	70, 67
	Isorhamnetin-3-O-glucoside	–	15.6–8.85 µg/g	–	+	66, 67
	Quercetin-3-O-glucoside	–	2.41–1.33 µg/g	–	–	22, 66
Flavanone glycosides	Naringenin-7-O-glucoside	–	22.1–6.84 µg/g	–	–	22, 66
	Eriodictyol-7-O-glucoside	–	1.60–0.808 µg/g	–	–	22, 66
Flavonol aglycones	Kaempferol	+	1.71–1.96 µg/g	–	–	69
	Quercetin	–	1.78–1.43 µg/g	–	–	66
	Quercitrin	+	+	–	–	67
Sterols	Stigmasterol	+	18.9 µg/g	–	–	71
	β-Sitosterol	+	16.0 µg/g	–	–	71

Hint: Whereas (+) Present, (–) Absent

Nutritional Value: Almond is a valuable dietary source of lipid (comprising mainly monounsaturated fatty acids), protein, dietary fiber, vitamins E, minerals, phenolic compounds and phytosterols [25, 26, 27, 28]. The detailed nutritional composition of *Prunus amygdalus*is given in **Table 2.**

TABLE 2: BIBLIOGRAPHIC INFORMATION ON THE NUTRITIONAL COMPOSITION OF *PRUNUS AMYGDALUS*

Nutritional value per 100 g (3.5 oz)	
Energy	2,423 kJ (579 kcal)
Carbohydrates	21.6 g
Starch	0.7 g
Sugars	4.4 g
Lactose	0.00 g

Dietary fiber	12.5 g
Fat	**49.9 g**
Saturated	3.8 g
Monounsaturated	31.6 g
Polyunsaturated	12.3 g
Protein	**21.2 g**
Tryptophan	0.214 g
Threonine	0.598 g
Isoleucine	0.702 g
Leucine	1.488 g
Lysine	0.580 g
Methionine	0.151 g
Cystine	0.189 g
Phenylalanine	1.120 g
Tyrosine	0.452 g
Valine	0.817 g
Arginine	2.446 g
Histidine	0.557 g
Alanine	1.027 g
Aspartic acid	2.911 g
Glutamic acid	6.810 g
Glycine	1.469 g
Proline	1.032 g
Serine	0.948 g
Vitamins	**Quantity% DV**
Vitamin A equiv.	0%
beta-Carotene	1 µg
lutein zeaxanthin	1 µg
Vitamin A	1 IU
Thiamine (B1)	18% 0.211 mg
Riboflavin (B2)	85% 1.014 mg
Niacin (B3)	23% 3.385 mg
Pantothenic acid (B5)	9% 0.469 mg
Vitamin B6	11% 0.143 mg
Folate (B9)	13% 50 µg
Choline	11% 52.1 mg
Vitamin C	0% 0 mg
Vitamin D	0% 0 µg
Vitamin E	171% 25.6 mg
Vitamin K	0% 0.0 µg
Minerals	**Quantity% DV**
Calcium	26% 264 mg
Copper	50% 0.99 mg
Iron	29% 3.72 mg
Magnesium	75% 268 mg
Manganese	109% 2.285 mg
Phosphorus	69% 484 mg
Potassium	15% 705 mg
Selenium	4% 2.5 µg
Sodium	0% 1 mg
Zinc	32% 3.08 mg
Other constituents	**Quantity**
Water	4.4 g

Protein: The protein-rich fraction of almond seeds is known as amandin and placed under legumin class, a major component of the globulin protein family [29, 30]. The concentration of Amandin protein content is approximately 70% of the total soluble globular proteins. Amandin consists of a hexameric structure, and each subunit is made up of two polypeptides chain-A (45 kDa) and chain-B (20 kDa) connected by a disulfide linkage with a molecular weight of 450 kDa (31).

Amandin and 2S albumin, are the glutamine-rich part of the protein and are responsible for the food allergy reactions seen in a few individuals who have intake almonds daily [32, 33].

Lipids: Lipids are made up of triacylglycerides of higher fatty acids in the body tissues and arranged in the form of phospholipids monolayer in which oleosins and integral proteins are embedded [34]. As compared with other tree nuts lipids, the kernel of almond is a rich source of saturated higher fatty acids with a prominent proportion of monounsaturated higher fatty acids (31.55%), polyunsaturated higher fatty acids (12.33%), along witha little amount of oleic acid [35, 36].

Carbohydrates and Dietary Fiber: The 26% carbohydrates, 12 % dietary fiber, 6.3 % sugars, 0.7 % starch, and other monosaccharides are the major component of the sweet almond kernel and its cell wall [37, 38, 39]. Additionally, the precise chemical composition and specific arrangement of the polysaccharides and non-saccharides in the cell walls have not been properly described. Various chemical compositional investigations have reported that the almond cell walls andthe almond kernel is made up of polysaccharides followed by gas-liquid chromatography analysis. It was confirmed that the major ingredients of the cell wall are uronic acid, arabinose, glucose, xylose, and galactose, which indicates that the cell wall is made up of arabinose-rich polysaccharides, including pectic material [40, 41]. A study suggests that the cell walls of almond testaare rich sources of sugar moiety glucose, xylose, arabinose, galactose and galacturonic acid but they vary from those in the cotyledon mannose, rhamnose and fructose are also part of their composition [42, 43, 44].

Micronutrients: Micronutrients are an integral part of the almond seeds and kernel. The kernel is a major source of vitamins such as vitamin E (tocopherols), vitamin B2 (riboflavin) along micronutrients such as calcium, potassium, zinc, magnesium, phosphorus, copper, manganese *etc* [45].

Vitamins: According to the survey by the U.S. Food and Drug Administration (FDA), almond seeds are placed under a rich source of multivitamins and minerals such as α-Tocopherol (vitamin E), Retinol (vitamin A), Thiamine (vitamin B1), Riboflavin (vitamin B2), Niacin (vitamin B3), Pantothenic acid (vitamin B5), pyridoxine (vitamin B6), Ascorbic acid (vitamin C), Vitamin D(Calciferol) and manganese *etc.* [46].

Sweet and Bitter Almond: There are two common species of almonds, namely, Sweet almonds (*Prunus amygdalus* Dulcis) and bitter almonds (*Prunus amara*). Important cyanogenetic glycosides called amygdaline and prunasin can distinguish the bitter almond from the sweet almond which is reported in its seed kernel[47]. Amygdaline is decomposed by the enzymatic hydrolysis into glucose and the harmful chemicals hydrocyanic acid (HCN) and benzaldehyde, known as cyanide poisoning [48]. The pharmacological importance of bitter almonds in respect to the anticancer and antibacterial properties is discussed in table 3 and table 4, respectively.

TABLE 3: ANTICANCER POTENTIAL OF BITTER ALMONDS AND AMYGDALIN

Cancer types	Novel medicinal agent/Bioactive	Dosage	Mode of action	Ref.
Colon cancer	Amygdalin	0.25-5 mg/ml	Down-regulation of cell cycle-related genes in SNU-C4 human colon cancer cells	72
Breast cancer		2.5-80 mg/mL	Amygdalin inhibited proliferation of MCF7, MDA-MB-231, andHs578T cells (IC50 values of amygdalin in MCF7, MDA-MB-231, andHs578T cells were 30.8, 48.5 and 52.9 mg/mL, respectively); regulated apoptosis-related proteins and signaling molecules; also inhibited adhesion of Hs578T cells	73
Bladder Cancer		1.25-10 mg/	Amygdalin reduced growth and proliferation in a dose-dependent manner in all studied bladder cancer cell lines by delaying cell cycle progression and G0/G1 arrest	74
Cervical cancer		1.25-20 mg/mL	Inhibited the growth of HeLa cell xenografts through a mechanism of apoptosis	75
Prostate cancer		0.01-10 mg/ml	Cancer cells by caspase-3 activation through down-	76

Lung cancer		2.5-5 mg/ml	regulation of Bcl-2 and up-regulation of Bax Amygdalin was likely to have an anti-metastatic NSCLC effect	[77]
Breast carcinoma cell line (MCF-7)	Aqueous extract		Cytotoxicity activity (IC_{50}= 29.5 µg)	[78]
Colon carcinoma cell line (HCT-116)	Ethanolic extract Methanolic extract	1.56-50 µg/ml	Cytotoxicity activity (IC_{50}= 31.4 µg) Cytotoxicity activity (IC_{50}= 45.7 µg)	
Hepatocellular carcinoma cell line (Hep-G2)	Ethanolic extract Methanolic extract Ethanolic extract		Cytotoxicity activity (IC_{50}= 39.4 µg) Cytotoxicity activity (IC_{50}= 10.1 µg) Cytotoxicity activity (IC_{50}= 17.4 µg)	

TABLE 4: ANTIBACTERIAL PROPERTIES OF BITTER ALMOND EXTRACT

Type of Microorganism	Extract type	Minimum inhibitory concentration (MIC)
Bacillus subtilis ATCC 6633	Aqueous	2.5 mg/ml
	Methanolic	0.625 mg/ml
	Ethanolic	2.5 mg/ml
Staphylococcus aureus NCTC 7447	Methanolic	1.25 mg/ml
	Ethanolic	10 mg/ml
Salmonella typhi NCIMB 9331	Methanolic	5 mg/ml

Pharmacology: *Prunus amygdalus*is the most common traditional nut tree famous for folkloric implications against several types of ailments and diseases. Apart from its nutritional value and almond exhibits various types of significant pharmacological activities due to the presence of numerous active biochemicals. A detailed summary of the several types of pharmacological findings is described below.

Antioxidant Action: A study demonstrates that the methanolic extracts of almonds fruits exhibit remarkable antioxidant and antiradical activities. Phenolic extract may help retard oxidative stress-related diseases. Four almond species were selected for the comparison between antioxidant and the antiradical activity of almond hull and phenolic extracts of the shell.

The methanolic extracts of these fruits were prepared from their hulls and shells, and the total phenolic and flavonoid content was calculated by using the Folin-Ciocalteureagent. The extracts' reducing capacity and scavenging potential for radical nitrite, hydrogen peroxide, and superoxide were investigated at various concentration levels. It was found that the almond hull gives remarkable antioxidant and antiradical activities compared to its shell phenolic extract and positively correlated with the phenolic content and radical scavenging capacities of the wild almond hull and shell extracts in different species [49].

Immuno-stimulant Action: A study suggests that almonds have a capacity for the production of plenty of cytokine production, *i.e.*, interleukins (IL-12), interferon-α (INF-α), INF-gamma, and tumor necrosis factor (TNF-α), *etc*. The above study claimed that almonds could significantly boost the immune surveillance of the peripheral blood mononuclear cells against the *Herpes simplex* virus (HSV-2) and other viral diseases [50].

Wound Healing Activity: A lot of natural gum oozes out from almond trees and shrubsat minimum maintenance cost, potentially used in food and pharmaceutical industries. Chemically, almond gum is composed of oligosaccharides (monosaccharides such as galactose and arabinose with traces of xylose and rhamnose) purified by enzymatic reactions. The detailed analysis was assessed by using a gas chromatography-flame ionization detector. The glycosyl bonding was characterized by using gas chromatography-mass spectrometry. It was reported that the principal chain is made up of galactose units [→3)-Gal-(1→] and is directly connected with arabinose residues [Ara-(1→]. The significant wound healing activity was investigated on the biosynthesized oligosaccharides on experimental rats. The potency

of oligosaccharides was analyzed by measuring the percentage of wound closure, reaching around 100% when applied alone or supplemented to the ointment formulation. It was noticed that the percentage healing capacity for the control group was mainly 74.3% on the same day. The histopathological examination of skin was visualized by light, digital microscopy revealed that collagen tissue deposition gets improves and enhances fibroblast cells and vascular densities [51].

Prebiotic Potential: Prebiotics induces the growth of beneficial microorganisms in our body. Almond seeds and hulls are a rich source of potential prebiotics. The present study was compared the *in-vitro* fermentation and *in-vivo* prebiotic potential of raw as well as roasted almonds. In an *in-vitro*, studies revealed that raw and roasted almonds can facilitate the growth of microorganisms *Lactobacillus acidophilus* (La14) and *Bifidobacterium breve* (JCM 1192). After the subsequent four-week observation, a daily intake of raw or roasted almonds promoted the growth of JCM 1192 and La14 colonies and arrested the growth of *Enterococcus* spp. in feces and caecal contents of rats.

Raw almonds had a remark ablebifido bacteria promotion effect as compared with roasted almonds, whereas prominent higher β-galactosidase activity and lower β-glucuronidase and azoreductase activities in feces contents of rats were reported with raw almonds as compared to roasted almonds. Thus, in terms of metabolic effects, the daily utilization of roasted almonds gives remarkable gut lipase activities. It was concluded that both raw and roasted almonds give a significant prebiotic activity and promote the intestine's metabolic activities. During the roasting, it may decrease the prebiotic potential of almonds but significantly enhance the metabolic action [52].

A new *in-vitro* study suggests that the almond seed exhibits a promising prebiotic effect on mixed fecal bacteria cultures. Finely ground almonds (FGA) and defatted finely ground almonds (DGA), were selected for *in-vitro* study by the combined model of the GIT, which included an *in-vitro* colonic model influence on the composition and metabolic activity of gut bacteria populations.

FGA potentially enhances the populations of *bifidobacteria* and *Eubacterium rectale*, with a higher prebiotic index (4.43) as compared to commercial prebiotic fructooligosaccharides (4.08) at 24 h of incubation. The increase in the population of *Eubacterium rectale* during the fermentation process of FGAdirectly correlated with several butyrate productions. Thus it was concluded that the addition of FGA changes the composition of intestine bacteria by facilitating the growth and development of *bifidobacteria* and *Eubacterium rectal* [53].

Hypoglycaemic Action: A study suggests that consumption of almond nut was investigated by Adventists study the nurse's health study, the physician's health study, the health professionals study, and the Iowa women's health study can decrease the postprandial glycemia, insulinemia, and oxidative stress in healthy individuals. Seven men and eight women (15 healthy individuals) 26 to 34 years old were selected for such study. The subjects consumed the control meal on 2 occasions and only once the almond, parboiled rice, and mashed potato meals. The blood glucose level was monitored after the four hours for each meal suggests that the almond and rice meal gives lesser values than the instant mashed potato meal ($p \leq 0.003$). Similarly, the post-prandial glucose peak heights for the almond and rice meals were decreased than the peak heights for the potato meal and the control white bread ($P < 0.001$) [54].

An investigation revealed that the ethanolic extract of almond leaves, flowers, and seeds at a dose level of 250 and 500mg/kg was selected and administered for 21 days for anti-diabetic activity against normal streptozotocin-induced diabetic experimental mice for prominent reduction of blood glucose levels.

The blood glucose levels on the 15th day were recorded as 80.6±1.8 and 77.6±1.4 mg/dl in the diabetic experimental mice by the treatment of leaves extract at a dose level of 250 and 500 mg/kg body weight, respectively. Whereas the flower and seed extract, at a dose of 500mg/kg body weight, also exhibits a remarkable reduction of blood glucose levels ($P < 0.001$) on diabetic mice on the 15th day [55].

Aphrodisiac Action: Tentex Royal is a multi-ingredient herbal formulation along with *Prunus amygdalus* exhibits a significant aphrodisiac property. The assessment of the therapeutic efficacy of Tentex Royal was investigated by stimulating the male sexual response against virgin female rats having an estrous state stimulated by estrogen administration. The male rats were randomly divided into five groups, *i.e., the* control group, the sildenafil citrate used as the reference standard group, and the test group having Tentex Royal formulation at a dose level of 125, 250, and 500 mg/kg body weight, respectively for five days. Various parameters such as total sexual behavior, mounting frequency, ejaculation latency, ejaculation frequency, serum testosterone levels, and sperm count were observed very carefully. A potential improvement was noticed in context with the parameters mentioned above, along with testosterone levels of the sexual indices in the Tentex Royal group. Histological studies of the anterior pituitary observed an increase in the FSH-LH-producing basophils and decreased ACTH-producing cells. The current study suggests that the Tentex Royal can enhance the erectile capacity of male rats. Thus considering the limitations of sildenafil citrate in clinical practice, the Tentex Royal may be used as a safe and alternative aphrodisiac herbal formulation and can significantly enhance the erectile capacity [56].

Hepatoprotective Action: A new study was carried out that methanol: ethanol (70:30) extract of almond fruit (150mg/kg and 300mg/kg) gives promising hepatoprotective activity against Paracetamol and CCl_4induced hepatitis in experimental rats. Paracetamol (2g/kg) and CCl_4(1.5ml/kg) increase the hepatic damage such as SGPT, SGOT, ALP, total bilirubin, direct bilirubin, and the tissue levels of GSH. Thus the treatment with the extract of the Prunus fruits can alter the levels of the biochemical markers to near-normal levels in a dose-dependent manner [57].

A preclinical study, suggests that rats who administered almond oil before the CCl_4treatment had potentially reduced the ALT (serum alanine aminotransferase), AST (aspirate aminotrans ferase), ALP (alkaline phosphatase), LDH (lactate dehydrogenase activities), TC (total cholesterol), TG (triglyceride) and LDL (low-density lipoprotein) content and increased HDL (serum high-density lipoprotein) content. Whereas pretreatment with almond oil significantly enhances the SOD (hepatic superoxide dismutase), GPx (catalase and glutathione peroxidase, and MDA (decreased malondialdehyde) level of rat [58].

Neuroprotective Activity: The current study investigated theneuroprotective effect of *Prunus amagdylus* nut kernels against aluminum chloride-induced spatial memory deficits in rats. Plant material was extracted, and extracts were evaluated for antioxidants by the DPPH method. Animals were classified into four groups, and each group contained five animals. Group 1 was normal and was kept undisturbed. Group 2 was administered with Aluminium Chloride (4.2mg/kg *i.p*) for 21 successive days. Groups 3 and 4 were pre-administered with *Prunus amygdalus* methanolic extract at doses 0.5 and 1mg/kg/ *p.o*) one hour before aluminum chloride administration. The memory parameters (acquisition and retrieval) were evaluated using the Morris water maze. After behavioral studies, the animals were sacrificed by decapitation and measured brain tissue thiobarbituric acid reactive substances (TBARS), glutathione (GSH), and catalase activity. Brain tissues from all the groups were histopathologically evaluated using Haematoxylin-eosin staining.

Administration of Aluminium chloride resulted in severe memory deficits and neurochemical alterations as was indicated by a significant increase in Transfer Latency time on Morris water maze and an increase in the brain tissue TBARS levels in the control group animals. A significant reduction in the GSH and catalase levels indicated decreased antioxidant defense. Histopathologically, the control group animal brain tissue showed signs of neuroinflammation. All behavioral and neurochemical, and histopathological changes were prevented to a significant extent in the animal groups pre-treated with *Prunus amygdalus* extract. Methanolic extract of *Prunus amaygdalus* possesses protective activity against aluminum chloride-induced neurotoxicity and associated memory deficits [59].

Antibacterial Activity: Natural antioxidants play an avital role as a defense mechanism in our body against reactive oxygen species (ROS) generation

and neutralizing their toxic effects. Most of the antioxidants are derived from natural as well as dietary sources and formulations having significant free radical scavenging properties due to the presence of secondary metabolites. The current studies determine the total phenolic content and investigate the in-vitro antibacterial and the antioxidant potential of almond leaves in variousnon-polar to polar solvents. It was concluded that almonds leaves were placed under the category of potent natural antioxidant and antimicrobial agent and promoted the utilization in pharmaceutical and food industrial application. However, further detailed studies are required to isolate the compounds from fresh and dried leaves that may be responsible for the same activities [60].

Nootropic and Hypophagic Effects: From time to time, interest is increasing in the finding of potential agents from natural as well as dietary sources for the proper maintenance of general health, management, and treatment of several ailments. Almonds fruits are a rich source of all the minerals traditionally used to enhance and sharpen memory and reduce blood cholesterol levels to avoid cardiovascular risk factors. The current study was carried out to evaluate the nootropic activity of almonds by Elevated Plus Maze and Radial Arm Maze test. The oral treatment of almonds was also monitored on food intake and plasma cholesterol levels in Rats. An almond paste was administered orally for 28 days and estimated Brain tryptophan, 5-HT and 5-HIAA at the end of the treatment. A promising enhancement in learning and memory of almond-treated rats was observed as compared to the control group. Almond-treated rats also show a remarkable reduction in daily food intake and blood cholesterol levels while the growth rate changes. Analysis of brain tryptophan monoamines suggests that tryptophan levels were increased and serotonergic turnover in rat brain due to daily oral intake of almonds. The above studies suggest that almonds give a promising hypophagic and nootropic action [61].

Hyperlipidemia: A recent study confirmed that the effect of sweet almond (*Prunus amygdalus*) suspension exhibits a significant induction the hyperlipidemia in male albino mice by the addition of 1% cholesterol to the routine diet along with 0.5% hydrogen peroxide into the drinking water, with *ad libitum* both food and water for sixty consecutive days. Serum lipid profile (total cholesterol level [TC], triacylglycerol level [TAG], low-density lipoprotein cholesterol [LDL-C], very LDL-C [VLDL-C], and high-density lipoprotein cholesterol [HDL-C]) was also measured. Prothrombin time, partial thromboplastin time, and clotting time potentially increased only in test groups treated with almond suspension and compared with the positive control group. The total blood platelet counts remarkably decreased in almond suspension-treated groups. The serum levels of TC, TAG, LDL-C, and VLDL-C in the *Prunus amygdalus* suspension treated groups at a dose level of 857, 1128, and 1428 mg/kg significantly decreased, whereas the serum level of HDL-C potentially increased as compared with the positive control group. Oral treatment at a dose of 1428 mg/kg body weight of *Prunus amygdalus* suspension significantly decreases the Serum lipid profile. It promotes prothrombin time, partial thromboplastin time, clotting time, and serum level of HDL-C in experimentally induced hyperlipidemic mice [62, 63].

Preclinical and Clinical Studies: Several types of investigations approved that *Prunus amygdalus* Batsch (almond) is globally used as classical nutritive traditional medicine. The nutrition value and antioxidant properties of almonds are clinically approved as a potent antioxidant along with the treatment of various disorders. Another study scrutinized the renal protective effect of *Prunus amygdalus* seed coat extract, and its underlying mechanism in an experimental animal model of Ferric nitrilotriacetate (Fe-NTA) induced renal cell carcinoma (RCC). The therapeutic efficacy of almonds treatment was screened by changes in biochemical parameters, renal, macroscopical, and histopathological parameters. Moreover, interleukin-6, tumor necrosis factor-α, interleukin-1β, and inflammatory mediators including prostaglandin E2, nuclear factor-kappa B were also determined to explore the exact mode of action. Thus, it can be concluded that almonds exhibit significant chemo-protective action and effect on ferric nitrilotriacetate-induced renal cell carcinoma via dual inhibitory action, one by retarding free radical production and the second by preventing inflammation [64]. A new study found the therapeutic efficacy and safety of all-day moisturizing,

polyherbal cream for the topical application on photosensitive, dry, and scaly skin. A polyherbal formulation contains several types of natural ingredients such as *Prunus amygdalus*, *Saccharum spontaneum*, *Hedychium spicatum*, and *Alpinia galanga*, in various concentrations having emollient, anti-infective, antioxidant, and anti-allergic properties were studied for its skin moisturizing effects. A clinical and preclinical assessment by the dermatologist was investigated, and baseline values concerning the moisture content of 50 or less recorded using the Moist Sense instrument were considered for the detailed study [65].

Future Prospects: In the last decades, it was noticed that traditional medicinal plants biosynthesize several types of potent novel medicinal agents that play an important role in treating several types of diseases and ailments. Nowadays, about 90% of potent agents are placed under the newly discovered pharmaceuticals. Traditional medicine provides health coverage for over 80% of the global population, especially in developing countries. An extensive literature survey on *Prunus amygdalus* revealed that these plants contain many dietary supplements and active novel medicinal agents with significant antioxidant, anti-diabetic, hepatoprotective, radiation protective, neurological disorder, anticancer activities, and many more. These activities make this medicinal plant a unique candidate to write a review and provide useful information to researchers. Thus the application and contributions of *Prunus amygdalus* in advancements of the therapeutic and nutritional value and emerging new avenues by providing novel applications and a new vision for the future are outlined. This review will open new doors for this molecule to be explored further in the form of formulation and clinical trial studies.

CONCLUSION: Global interest in the investigation of natural herbs and traditional medicines is increasing day by day due to novel medicinal agents having promising pharmacological values and their ability to treat various diseases. A wide range of plant-derived phytomedicine has entered the global market due to its medicinal importance and explores globally for the utilization and treatment of several diseases. Similarly, *Prunus amygdalus* is a versatile plant cultivated all over the world with a plethora of nutritional and medicinal value. Almondsareari chsource of minerals and a wide range of phytochemicals such as aldehydes and hydroxybenzoic acids, flavanones, is flavones, flavonol, phenolic acids, flavan-3-ols, and lignans with diverse medicinal importance. Thus, it is concluded that there is a wide scope for scientific investigations to explore its nutritional and medicinal value to claim the traditional use and explore novel and promising lead compounds from almonds. In the current review, the authors are trying to present and compile all major information related to its phytochemical and pharmacological behavior and its nutritional importance published till now.

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