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Review Paper

Kashmiri famous fruit Apple (*Malus domestica*): Review of nutritional value, phytochemical constituents and pharmacological properties

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ABSTRACT

A beautiful shape, appealing color, and very good taste make apples the "king of delicious fruit". Apples are typically eaten as fresh fruit but are commonly found in processed food products. Among the most well-liked fruits, apples are especially abundant in bioactive chemicals like flavonoids and are a good source of nutrients. The goal of this article is to provide sufficient information about apples for use in herbal medicine research, including their shape, nutrient content, chemical compound, and pharmacological characteristics. Published articles were surveyed using Pub Med, Medline, Science Direct, Google Scholar, and other search engines to study *Malus domestica* (apple), a well-known fruit. Pharmacological studies on *Malus domestica* have confirmed its antioxidant, anti-dyslipidemic, antidiabetic, anti-cancerous, anti-proliferative, anti-obesity, cardiovascular protective, antimicrobial, anti-inflammatory, cognitive, and gastroprotective activity, etc. Fresh apple is also good for energy (50 Kcal/100g). The goal of this review is to explore the fruit's purported pharmacological efficacy, chemical makeup, and nutritional value. When dealing with this fruit, scientists, researchers, and other health experts will find it useful as a reference with the most recent information available.

Keywords: Antidiabetic; antioxidant; apple; king of fruit; *Malus domestica*; phytochemicals

The World Health Organisation (WHO) estimates that 65–80% of people worldwide rely on traditional medicines to meet their basic medical needs (Khan *et al.,* 2023). In the present era, most individuals prefer medicines made from plant, leaf, fruit, or seed extracts due to the extremely low or non-existent side effects and place more emphasis on healthy eating. (Chakraborty *et al.,* 2023). Fruits are essential to maintaining a healthy lifestyle because they are the main dietary source of micronutrients (vitamins and minerals) and phytonutrients (e.g., antioxidants) (Sharma *et al.,* 2014). *Malus domestica* comprises the term from the Latin "Malus", which implies "evil or apple" Moreover the feminine nominative of "domesticus," is"domestica." (Chakraborty *et al.,* 2023). Botanically, apples are of the genus Malus and family Rosaceae, which is categorized as pome fruits. (Wolfe *et al.,* 2003). Using the adage "An apple a day keeps the doctor away," Hippocrates asserted that apples, the most popular fruit, provide numerous health benefits (Chakraborty *et al.,* 2023). Apples are typically eaten as fresh fruit but are also frequently seen in prepared food items. A few common examples of apple-based processed goods are wine, apple cider vinegar, apple pies, sauces, jams, and apple nibbles (chips). There are numerous byproducts produced during the processing of apples. Pomace is the name given to this by-product, which is made up of a variety of soft tissue, calyx, seed, peel, and core (Asma *et al.,* 2023).

Methodology: *Malus domestica* the famous fruit was surveyed for its morphology, nutritional values, phytochemical constituents, uses, and other related concepts from published articles. The internet sources for the information were also searched using the keywords *Malus domestica*, Phytochemicals, etc. PubMed, Medline, Science Direct, Google Scholar, and other search engines were referred for the reported activities

and reviews about *Malus domestica*. Papers from between 1997 and 2023 were included. The observations were noted, analyzed, and compared to collate the information that is only focused on *Malus domestica* in the form of this review study.

Fruit description: ***Origin and Habitat:*** Growing in Asia and Europe since the dawn of written history, apples are among the popular temperate fruits. As far back as 6000 BC, apples were known to have existed. The cornerstone and foundation of Kashmir's temperate fruit sector is the apple, the most important horticultural fruit crop (Darzi, 2016). Kashmir apples are grown in higher hilly terrains between 1600 and 2500 meters over the sea level. Except for species cultivated in the Nilgiris, which are harvested from April to July, they require a temperature that is sufficiently cold for production, thus they are harvested in late August. It takes 130-150 days following full flowering (Chakraborty *et al.,* 2023).

Morphological Characteristics: Dicotyledonous, annual, and deciduous, apple trees under cultivation range in height from 2 to 4.5 meters and have oval, dark green alternately arranged leaves with serrated edges that are between 3/4 and 2 inches wide and 1-3 inches in length. Its springtime blooms consist of an inflorescence that consists of a central flower called "King Bloom" and a cyme with four to six blossoms. The flowers are white with five petals and are 3–4 cm across. Fruits are colorful and juicy, with hues ranging from red to green to yellowish-red, and others, with diameters of 5 to 9 cm. The fruit's fleshy thalamus section can be consumed. Apple flesh, often referred to as exocarp, is a light yellow or yellowish-white color. The fruit's center is composed of five carpels, each of which contains two to three seeds. Apple seed is non-endospermic and propagates through epigeal germination. Each seed is a tiny oval shape, black in color, 0.3 inches long, 1/4 inches wide, around 1/8 inches thick, and mildly toxic (Chakraborty *et al.,* 2023; Wolfe *et al.,* 2003). Fall is the season for picking mature fruits. The fruit's skin has an epicuticular wax layer that serves as a barrier against transpirational losses. (Amarante *et al.,* 2008).

Synonyms: Its synonyms are Tsoonth (Kashmiri), Apple (English), Sev (Hindi, Oriya), Safarjan (Gujarati), Sebu (Kannada), Epal (Malayalam), and Safar Chad (Marathi) (Lobo *et al.,* 2018; Chakraborty *et al.,* 2023).

Taxonomical Classification*:* Domain: Eukaryota, Kingdom: Plantae, Phylum: Spermatophyta, Subphylum: Angiospermae, Class: Dicotyledonae, Order: Rosales, Family: Rosaceae (Rose family), Genus: Malus, Species: M. domestica, Binomial Name: Malus domestica (Azizah *et al.,* 2020; Chakraborty *et al.,* 2023).

Table 1: Nutritional value per 100g of fresh apple constituents

Constituents	Values
Water	85.56 g
Energy	52 Kcal
Carbohydrate	13.81 g
Sugar	10. 39 g
Dietary fibre	2.4 g
Protein	0.26 g
Fat	0.17 g
Pectin	0.5 g
Potassium	107 mg
Phosphorus	14 mg
Calcium	6 mg
Magnesium	5 mg
Vitamin C	4.6 mg
Sodium	1 mg
Iron	0.12 mg
Copper	0.03 mg
Thiamine (B1)	0.017 mg
Riboflavin (B2)	0.026 mg
Niacin (B3)	0.091 mg
Carotene	45 ug
Folate	3 ug
Cholesterol	0 mg

Nutritional value: Apple is categorized as a sub-acid food (3.5–6.5). The Major Constituents of fresh Apples per 100g according to USDA 2015 are presented in Table 1. (Chaudhary *et al.,* 2014; Lobo *et al.,* 2018; Jiri *et al.,* 2020; Azizah *et al.,* 2020; Hamid *et al.,* 2020).

Phytochemical constituents: The main natural source of phytochemicals is apples. Apples are abundant in polyphenols, which are a collective name for flavonoids and other phenolic compounds (Sun *et al.,* 2002). The main flavonoids present in apples are flavonols(71-90%), flavanols-3-ols(1-11%), chalcones/dihydrochalcones(2-6%), andanthocyanins (1-3%). In apples, quercetin glycosides (such as quercetin 3-glycoside) are the most common flavonols. The major compounds belonging to flavanols are catechins, epicatechins, and procyanidin B2 (they are mostly found in apple pulp and peel). Anthocyanins include gallic acid, coumaric acid, chlorogenic acid, and cyanidin 3-galactoside, which is the most prevalent anthocyanin and gives red apple peel its red color. Phlorizin and phloretin are phenolic compounds

associated with dihydrochalcones. Mainly found in conjugated forms, these chemicals are more commonly found in apple pomace and seeds (related to fruit sugar content, like xyloglucan and glucose). (Asma *et al.,* 2023; Jiri *et al.,* 2020; Azizah *et al.,* 2020; Hamid *et al.,* 2020). Flavanols comprise almost 80% of the polyphenols found in apples, which are followed by hydrocinnamic acid and chlorogenic acid (Sun *et al.,* 2002). The compounds that are most commonly found in apple peels are procyanidins, epicatechin, catechin, phloridzin, chlorogenic acid, and quercetin conjugates. There is some epicatechin, procyanidin, phloridzin, and catechin in apple flesh, but they are present in much lower concentrations than in the peels. The flesh often contains more chlorogenic acid than the peel. Recent studies have demonstrated that apple peels have two to six times as many phenolic chemicals and two to three times as many flavonoids as apple flesh (Lobo *et al.,* 2018).

The pharmacological activity of Apple: Apples have been found to exhibit a wide range of pharmacological effects, which can be divided into the following categories due to the presence of several bioactive components.

Anti-oxidant activity: The consumption of apples stimulates the activity of antioxidant enzymes such as glutathione peroxidase and superoxide dismutase (SOD), which improves blood serum's antioxidant capacity (Eberhardt *et al.,* 2000). The antioxidant chemicals found in apples that have been studied the most include procyanidin, cyanidin-3-galactoside, coumaric acid, gallic acid, phloridzin, catechin, rutin, epicatechin, quercetin-3-galactoside, glucoside, and rhamnoside. (Lobo *et al.,* 2018). 100 g of apples have antioxidant activity equal to approximately 1500 mg of vitamin C (Boyer & Liu, 2004). Furthermore, it has been observed that 100 g of apples has eight times more antioxidant activity than apricots and three times more than oranges (Persic *et al.,* 2017). Following reports that 100 grams of apples contain approximately 5.7 mg of vitamin C. This helps enhance immunity, rejuvenates skin, prevents pernicious anemia, and provides anti-aging effects. Higher levels of antioxidants have also improved sleep quality and reduced the risk of cardiovascular illnesses (Chakraborty *et al.,* 2023). The antioxidant activity of the peel is higher than that of the flesh (Sun *et al.,* 2002).

Anti-dyslipidemic activity: Apples' ability to lower cholesterol has been attributed to their soluble fiber content, antioxidants, and phenolic compounds, which are especially attributed to the 1%–1.5% pectin content of apples. Pectin lowers cholesterol levels by reducing insulin secretion and helps manage insulin levels by decreasing the release of sugar into the bloodstream (low glycemic index) (Lee, 2012; Mayer *et al.,* 2001). It has been found that apples reduce triglyceride, plasma, and liver cholesterol levels because they contain antioxidants and phytochemicals such as flavonoids, polyphenols, and carotenoids alone and in combination with soluble fibers (Leontowicz *et al.,* 2002). Regular apple consumption has been shown to reduce total blood serum cholesterol and LDL cholesterol due to their high soluble fiber content. Studies also indicate that consuming 5–10 g of soluble fiber from apples can reduce total cholesterol (Aprikian *et al.,* 2001).

Anti-diabetic activity: The inhibition of α-glycosidase has been helped by the presence of polyphenols such as dihydrochalcones (phloridzin), quercetin, proanthocyanidins (flavonoids), and Catechin (flavonols) in various fruit parts and seeds. Thus, by promoting the release of insulin from pancreatic cells through decreased oxidative stress-induced tissue damage, as well as by increasing glucose utilization in body cells and regulating the excess release of glucose from the liver, this way lowers the risk of postprandial hyperglycemia and insulin levels in pre-diabetics as well as in type 2 diabetics. Proanthocyanidins are the most potent polyphenolic substances, as studies have shown that they can block α-glycosidase by more than 90%. Moreover, dihydrochalcones phloretin-29-0 glucoside, which is found in apples in relatively large levels, inhibits intestinal lumen sodium-dependent glucose transporters, potentially lowering the postprandial glucose response (Richardson *et al.,* 2020; Chakraborty *et al.,* 2023; Oliviera *et al.,* 2003; Olthof *et al.,* 2003). According to research conducted in vivo, eating one apple a day reduces the risk of diabetes by 28% (Oliviera *et al.,* 2003).

Anti-cancerous activity: Both the peel and the flesh are high in flavonoids and polyphenols, which have anti-inflammatory and anti-cancer effects. Lung cancer incidence and flavonoid intake are substantially inversely correlated (Arts *et al.,* 2001). Chlorogenic acid in apples kills or inhibits the growth of human cancer cells in the colon, breast, and liver. According to a Cornell University study, flavonoids and polyphenols, particularly epigallocatechin gallate, cooperate to protect the body from free radical-induced oxidation and tissue damage. The fundamental mechanism behind apple consumption's ability to prevent cancer is by damaging DNA and thereby lowering the amount of big aberrant neural foci in the colon, which in turn

lowers important cancer markers (Boyer & Liu, 2004). Due to its cytotoxicity, the cyanogenic glycoside amygdalin is very effective at preventing the growth of cancerous cells. Additionally, this gives hope for the treatment of skin, lung, and cervical cancer in humans (Ci *et al.,* 2018). Apples with peels were more effective than apples without peels at reducing the development of cancer cells (Lobo *et al.,* 2018).
Prevention of cardiovascular diseases (CVD): The polyphenol (quercetin) and fiber (pectin) content of apples decrease LDL and total plasma cholesterol and prevent CVD. They prevent CVD by regulating lipid metabolism, inhibiting lipid peroxidation, lowering pro-inflammatory molecule synthesis, and reducing the accumulation of vascular cell adhesion molecules (VCAM-1 and VCM-1) (Sesso *et al.,* 2003; Thakur *et al.,* 1997). Approximately 10% of flavonoids, from the intake of apples, are strongly correlated with are reduced risk of CHD (Wolfe & Liu, 2003).

Anti-proliferative activity: Among fruits, apples have the third-highest anti-proliferative activity. Apple procyanidins function as chemo-preventive agents by either destroying harmful substances or preventing the production of polyamines. The polyphenol mixture stimulates chemo-preventive enzymes' gene expression (sulfotransferase and glutathione-S-transferases) (Liu & Sun, 2003). Polyphenols, phytosterols, polysaccharides, Pentacyclic triterpenes, primarily the cyanogenic glycoside amygdalin, found in various apple parts, are beneficial in preventing several common malignancies, including Hep-2 liver cancer and Caco-2 colon cancer, by blocking the type 2 glucose transporter (GLUT 2) (Jiri *et al.,* 2020).

Asthma and pulmonary function: There is a negative relationship between consuming apples and the risk of developing asthma in individuals due to the preventive impact of the antioxidants and phytochemicals (flavonoids) in apples (Shaheen *et al.,* 2001). According to a study by UK experts, Asthma risk can be lowered by one-third by eating at least two apples per day (Woods *et al.,* 2003). By lowering pro-inflammatory cytokines in plasma, apple consumption reduces inflammation of the airways and reduces neutrophils in asthmatics (Denis *et al.,* 2013).

Aging and cognitive processes: Apple-based products have demonstrated the capacity to inhibit presenilin1 protein synthesis, it acts as a mediator in the production of amyloid-B protein, a distinctive characteristic of Alzheimer's disease that is most common (Walle *et al.,* 2000). Normal cognitive function is improved by S-adenosyl methionine (SAM), a precursor to ripening hormones in apples (Crespy *et al.,* 2001). Eating an apple every day can help improve memory in Alzheimer's patients by reducing the loss of the neurotransmitter acetylcholine. (Dai *et al.,* 2006; Chaudhary *et al.,* 2014).

Anti-obesity activity: Apples' polyphenolic concentration increases skeleton bulk and brown fat. The mitochondria of the cells rapidly metabolize brown fat to release heat and energy and are therefore regarded as beneficial since they lower the risk of obesity and accumulation of white fat in the body (Oliviera *et al.,* 2003). It is believed that the satiety effect of apples' high fiber content contributes to weight loss. In the gut, it absorbs water and turns into a thick gel, which lowers hunger sensations and gives a feeling of fullness. This will lower the amount of food consumed, which will lower the total amount of calories consumed and encourage weight loss (Boyer & Liu, 2004; Knekt *et al.,* 2002).

Bone health: A medium apple provides 15% of the daily required intake of fiber and vitamins C and K. and many trace minerals and polyphenols that strengthen bones like potassium and magnesium, and flavonoids that enhance bone health and mineral density by producing alkaline metabolites that inhibit calcium from being excreted (Tucker *et al.,* 1999; Wariaghli *et al.,* 2010). Recent studies carried out in France have demonstrated that the flavonoid antioxidant phloridzin, which is particular to apples, can enhance inflammatory indicators in women after menopause, thereby reducing bone breakdown and increasing bone density. (Day *et al.,* 2003). It has also been proven that some apple polyphenols enhance osteoblast formation (Vinson *et al.,* 2001).

Gastrointestinal protection: Apples, especially those high in catechin and chlorogenic acid, shield the mucosal cells from oxidative damage. These phenolic compounds are thought to have a protective impact because they boost antioxidant activity and lower lipid peroxidation. Apple products mediate and scavenge nitrogen oxides, thereby lowering the risk of mutagenesis in stomach cancer and exerting a gastroprotective effect (Peri *et al.,* 2005). Additionally, studies conducted in vitro have demonstrated that many apple product-derived molecules have anti-ulcer properties. Apple peel extract, rich in carotenoid, has been demonstrated to inhibit H. pylori (Del Rio *et al.,* 2013).

Anti-microbial activity: The production of phenolic compounds (catechin and terpineol) from apple fruit extracts and seeds that are based on water or alcohol has shown efficacy in inhibiting the growth of gram-

positive and gram-negative bacteria, including S. aureus and E. coli, respectively (Oduwole *et al.,* 2020; Wojdylo *et al.,* 2020). The enzymatic activities of the cholera toxin were recently found to be suppressed by crude extracts from immature apples in a dose-dependent manner (Oliviera *et al.,* 2003).

Anti-inflammatory Properties: The anti-inflammatory properties of apple parts and seeds are a result of the prevention of injury to gastrointestinal tissues as seen by polyphenol chemicals and inactivation of NF-kB (Jiri *et al.,* 2020; Chakraborty *et al.,* 2023). Due to their antioxidant properties, which serve as metal ion chelators, singlet oxygen quenchers, ROS scavengers, and hydrogen-donating chemicals, apple polyphenol extracts have an anti-inflammatory impact that inhibits damage to human gastric epithelial cells in vitro and to rat stomach mucosa in vivo (Nouri *et al.,* 2011).

Toxicological Effects: Amygdalin (1-4mg/g of apple seeds) is present in apple seeds, and it has cytotoxic characteristics. When administered in the form of apple seed oil or correctly extracted, this cyanogenic glycoside seems to be quite beneficial in preventing different types of malignancy (Oduwole *et al.,* 2020; Wojdylo *et al.,* 2020).

Apples boost gum health: Apples are frequently referred to be nature's toothbrush. While biting and chewing on an apple stimulates the gums and increases saliva flow, eating an apple does not clean your teeth. This lowers the number of bacteria in the mouth and prevents tooth decay (Boyer & Liu, 2004; Chaudhary *et al.,* 2014; Boyer & Liu, 2004).

Boosts immunity: Quercetin has been shown in recent studies to strengthen and support your immune system, especially when you're under stress (Boyer & Liu, 2004; Chaudhary *et al.,* 2014).

Beat diarrhea and constipation: Apples can help both diarrhea and constipation, even though they are two quite different gastrointestinal disorders. The fiber in apples can absorb excess water in cases of diarrhea and extract water from your intestines while you're constipated (Chaudhary *et al.,* 2014).

Glowing skin effect: The fact that apples are excellent for the skin is one of the less well-known advantages of eating them. It contains a lot of antioxidants and vitamin C, which keep skin glowing and stave off wrinkles and other signs of aging (Aprikianet *et al.,* 2003; Chaudhary *et al.,* 2014).

Antacid activity: Due to the presence of pectin and the effect of glycine, it is ideally suited to reduce stomach acidity (Lobo *et al.,* 2018)

Diuretic and Depurative activity: Malic acid, cysteine, and arginine found in apples, are excellent for removing toxins from the body as well as for treating or preventing disease (Lobo *et al.,* 2018)

Hearing protection activity: Apple vinegar contains a lot of potassium, magnesium, zinc, and manganese and is good for the health of the ear because deficiency of these can cause deafness (Lobo *et al.,* 2018)

CONCLUSION

According to scientific studies and research, eating apples regularly may have beneficial therapeutic or nutraceutical benefits in the prevention of several diseases. Apples are a great source of vitamins, minerals, phytochemicals, and dietary fiber. Several epidemiological studies have related apple consumption to a reduced risk of chronic diseases, including diabetes, asthma, cancer, and cardiovascular disease. This association is also true for apple-based processed products and polyphenol-rich extracts. Studies conducted on animals and in vitro have shown that apples have strong antioxidant activity, which may account for their ability to reduce the risk of chronic diseases. They may also inhibit the growth of cancer cells, reduce lipid oxidation, and lower cholesterol. There is sufficient data to support some of the health-related effects, but a more thorough study is still required. To incorporate the therapeutic qualities of the various apple components in herbal medicine globally and minimize the toxic effects, further research and study on phytopharmacological properties should be conducted in depth. It will bring about benefits for the economy in addition to protecting human health.

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REFERENCES

Amarante, C.V., Steffens, C.A., Mafra, Á.L., Albuquerque, J.A., 2008. Yield and fruit quality of apples from conventional and organic production systems. *Pesquisa Agropecuária Brasileira,* **43**: 333–340.

Aprikian, O., Levrat-Verny, M.-A., Besson, C., Busserolles, J., Rémésy, C., Demigné, C., 2001. Apple favorably affects parameters of cholesterol metabolism and anti-oxidative protection in cholesterol-fed rats. *Food Chemistry*, **75**: 445–452.

Arts, I.C.W., Hollman, P.C.H., Bueno de Mesquita, H.B., Feskens, E.J.M., Kromhout, D., 2001a. Dietary catechins and epithelial cancer incidence: The Zutphen elderly study. *International Journal of Cance*r, **92**: 298–302.

Asma, U., Morozova, K., Ferrentino, G., Scampicchio, M., 2023. Apples and Apple By-Products: Antioxidant Properties and Food Applications. *Antioxidants,* **12**: 1456.

Azizah, P., Husnunnisa, Misfadhila, S., 2020. Review of phytochemical and pharmacological effects of apple. *International Journal of Research and Review,* **7**: 231-237.

Boyer, J., Liu, R.H., 2004. Apple phytochemicals and their health benefits. *Nutrition Journal,* 3: 1-15.

Chakraborty, A., Deb, J.S., Saha, M., Chatterjee, S., 2023. Apple seeds: phytochemistry, medicinal property, and toxicology. *Int J Pharm Sci & Res,* **14**: 1038-45.

Chaudhary, Dinesh, A., Chaudhary, Mahesh, R., Judal, Ashwin, L., 2014. Apple: Varieties and its health benefits. *Res. J. Animal Hus. & Dairy Sci*, **5:** 35-38.

Ci, Z., Kikuchi, K., Hatsuzawa, A., Nakai, A., Jiang, C., Itadani, A., 2018. Antioxidant activity and α-glucosidase, αamylase, and lipase inhibitory activity of polyphenols in flesh, peel, core, and seed from mini apple. *American J of Food Science and Technology,* **6:** 258–262.

Crespy, V., Aprikian, O., Morand, C., Besson, C., Manach, C., Demigne, C., Remesy, C., 2001. Bioavailability of phloretin and phloridzin in rats. *The Journal of Nutrition,* **131**: 3227–3230.

Dai, Q., Borenstein, A.R., Wu, Y., Jackson, J.C., Larson, E.B., 2006. Fruit and vegetable juices and Alzheimer's disease: The Kame Project. *American J. Medi,* **119**: 751- 759.

Darzi, M. I., 2016. Horticulture sector towards economic development of Jammu & Kashmir. *Multidisciplinary Research and Development,* **3**: 238–240.

Day, A. J., Gee, J. M., DuPont, M. S., Johnson, I. T., Williamson, G., 2003. Absorption of quercetin-3-glucoside and quercetin-4-glucoside in the rat small intestine: The role of lactase phlorizin hydrolase and the sodium-dependent glucose transporter. *Biochemical Pharmacology*, **65**: 1199–1206.

Del Rio, D., Rodriguez-Mateos, A., Spencer, J. P., Tognolini, M., Borges, G., Crozier, A., 2013. Dietary (poly) phenolics in human health: Structures, bioavailability, and evidence of protective effects against chronic diseases. *Anti-Oxidants Redox Signaling,* **18**: 1818–1892.

Denis, M. C., Furtos, A., Dudonné, S., Montoudis, A., Garofalo, C., Desjardins, Y., Delvin, E., & Levy, E., 2013. Apple peel polyphenols and their beneficial actions on oxidative stress and inflammation. *Plos One,* **8**: 53725.

Eberhardt, M., Lee, C., Liu, R. H., 2000. Anti-oxidant activity of apple peels. *Nature,* **405**: 903–904.

Hamid, M., Hassan, G.I., Wani, A.W., Mumtaz, S., Ashraf, S., Ahad, S., Wani, M.Y., Kumar, A., 2020. Physiology of flowering in Apple and almond: A Review. *International Journal of Current Microbiology and Applied Sciences,* **9:** 1912–1929.

Khan, F., Ansari, A.N., Nayab, M., 2023. Application of hot medicated fomentation for pain alleviation in non-specific low back pain - a randomized controlled clinical trial. *Journal of Bodywork and Movement Therapies,* **35**: 196–201.

Knekt, P., Kumpulainen, J., Järvinen, R., Rissanen, H., Heliövaara, M., Reunanen, A., Hakulinen, T., Aromaa, A., 2002. Flavonoid intake and risk of chronic diseases. *The American Journal of Clinical Nutrition,* **76**: 560–568.

Lee, C. Y., 2012. Common nutrients and nutraceutical quality of apples. *New York Fruit Quarterly,* **20**: 1–8.

Leontowicz, H., Gorinstein, S., Lojek, A., Leontowicz, M., Milan, Soliva-Fortuny, R., Park, Y.-S., Jung, S.-T., Trakhtenberg, S., Martin-Belloso, O., 2002. Comparative content of some bioactive compounds in apples, peaches, and pears and their influence on lipids and antioxidant capacity in rats. *The Journal of Nutritional Biochemistry,* **13**: 603–610.

Liu, R. H., Sun, J., 2003. The antiproliferative activity of apples is not due to phenolic-induced hydrogen peroxide formation. *Journal of Agricultural and Food Chemistry,* **51**: 1718–1723.

Lobo, A. R., Satish, S., Shabaraya, A.R., 2018. Review on pharmacological activities of Malus domestica. *Int J Pharm Chem Res,* **4**: 243–246.

Mayer, B., Schumacher, M., Brandstätter, H., Wagner, F.S., Hermetter, A., 2001. High-throughput fluorescence screening of antioxidative capacity in human serum. *Analytical Biochemistry,* **297**: 144–153.

Nouri, M. K., Rezapor, A. K., 2011. Effect of apple (Malus domestica) supplementation on serum lipids and lipoproteins level in cholesterol-fed male rat. *Middle East J. Sci. Res,* **9**: 744-748.

Oduwole, I., A, A., 2020. Amygdalin-therapeutic effects and toxicity. *Journal of Biotechnology and Biomedicine,* 3.

Oliviera, M., Sichieri, R., Moura, A., 2003. Weight loss associated with a daily intake of three apples or three pears among overweight women. *Nutrition,* **19**: 253–256.

Olthof, M. R., Hollman, P. C., Buijsman, M. N., Van Amelsvoort, J. M., Katan, M. B., 2003. Chlorogenic acid, quercetin-3-rutinoside, and black tea phenols are extensively metabolized in humans. *The Journal of Nutrition,* **133**: 1806–1814.

Patocka, J., Bhardwaj, K., Klimova, B., Nepovimova, E., Wu, Q., Landi, M., Kuca, K., Valis, M., Wu, W., 2020. Malus domestica: A review on nutritional features, chemical composition, traditional and medicinal value. *Plants,* **9**: 1408.

Peri, L., Pietraforte, D., Scorza, G., Napolitano, A., Fogliano, V., Minetti, M., 2005. Apples increase nitric oxide production by human saliva at the acidic pH of the stomach: A new biological function for polyphenols with a catechol group. *Free Radical Biology and Medicine,* **39:** 668–681.

Persic, M., Mikulic-Petkovsek, M., Slatnar, A., Veberic, R., 2017. Chemical composition of Apple Fruit, juice, and pomace and the correlation between phenolic content, enzymatic activity, and browning. LWT - *Food Science and Technology,* **82**: 23–31.

Richardson, A.T., Cho, J., McGhie, T.K., Larsen, D.S., Schaffer, R.J., Espley, R.V., Perry, N.B., 2020. Discovery of a stable vitamin C glycoside in crab apples (malus sylvestris). *Phytochemistry,* **173**: 112-297.

Sesso, H.D., Gaziano, J.M., Liu, S., Buring, J.E., 2003. Flavonoid intake and the risk of cardiovascular disease in women. *The American Journal of Clinical Nutrition,* **77:** 1400–1408.

Shaheen, S.O., Sterne, J.A.C., Thompson, R.L., Songhurst, C.E., Margetts, B.M., Burney, P.G.J., 2001. Dietary antioxidants and asthma in adults. American Journal of Respiratory and Critical Care Medicine, **164:** 1823–1828.

Sharma, P., Dhami, P., Pandey, P., 2014. Flavors of Apple Fruit—a review. *Journal of Nutritional Ecology and Food Research,* **2**: 288–291.

Sun, J., Chu, Y.-F., Wu, X., Liu, R.H., 2002. Antioxidant and antiproliferative activities of common fruits. *Journal of Agricultural and Food Chemistry,* **50**: 7449–7454.

Thakur, B.R., Singh, R.K., Handa, A.K., Rao, M.A., 1997. Chemistry and uses of pectin — a review. Critical *Reviews in Food Science and Nutrition*, **37:** 47–73.

Tucker, K.L., Hannan, M.T., Chen, H., Cupples, L.A., Wilson, P.W., Kiel, D.P., 1999. Potassium, magnesium, and fruit and vegetable intakes are associated with greater bone mineral density in elderly men and women. *The American Journal of Clinical Nutrition,* 69: 727–736.

Vinson, J.A., Su, X., Zubik, L., Bose, P., 2001. Phenol antioxidant quantity and quality in foods: *Fruits. Journal of Agricultural and Food Chemistry,* **49**: 5315–5321.

Walle, T., Otake, Y., Walle, U.K., Wilson, F.A., 2000. Quercetin glucosides are completely hydrolyzed in ileostomy patients before absorption. *The Journal of Nutrition*, 130: 2658–2661.

Wariaghli, G., Allali, F., Maghraoui, A.E., Hajjaj-Hassouni, N., 2010. Osteoporosis in patients with primary biliary cirrhosis. *European Journal of Gastroenterology & Hepatology,* 1.

Wojdyło, A., Oszmiański, J., 2020. Antioxidant activity is modulated by polyphenol contents in apples and leaves during fruit development and ripening. Antioxidants, **9**: 567.

Wolfe, K.L., Liu, R.H., 2003. Apple peels as a value-added food ingredient. *Journal of Agricultural and Food Chemistry*, **51**: 1676–1683.

Woods, R.K., Walters, E.H., Raven, J.M., Wolfe, R., Ireland, P.D., Thien, F.C., Abramson, M.J., 2003. Food and nutrient intakes and asthma risk in young adults. *The American Journal of Clinical Nutrition,* **78:** 414–421.