

## REVIEW ON PHARMACOLOGICAL ACTIVITIES OF *MALUS DOMESTICA*

Avrin Romitha Lobo<sup>1\*</sup>, Satish S<sup>1</sup> and AR. Shabaraya<sup>2</sup>

<sup>1</sup>Department of Pharmacology, Srinivas College of Pharmacy,  
Valachil, Post Farangipete, Mangalore-574143, Karnataka, India.

<sup>2</sup>Department of Pharmaceutics, Srinivas College of Pharmacy,  
Valachil, Post Farangipete, Mangalore-574143, Karnataka, India.

### ABSTRACT

*Malus domestica* distributes around 20 countries all over the world and normally in India, Asia, Africa, North & South America, and Europe. In India it is commonly seen in Uttaranchal appear during the late summer months, Jammu and Kashmir's apple season may stretch into late November. *Malus domestica* (Family - Rosaceae) are widely consumed, rich source of phytochemicals, and epidemiological studies have linked the consumption of apple with reduced risk of some cancer, cardiovascular disease, obesity, pulmonary dysfunction, asthma and diabetes. Apple has been found to have very strong antioxidant activity, inhibit cancer cell proliferation, decrease lipid oxidation, and lower cholesterol. The paper reviews on its pharmacological activities such as antiproliferative, anti-depressant, anti-inflammatory, anti-microbial.

**Keywords:** *Malus domestica*, Anti-inflammatory, Anti-oxidant, Antiproliferative, Anti-depressant.

### INTRODUCTION

WHO has listed over 21,000 plant species used around the world for medicinal purposes. In India, about 2500 plant species belonging to more than 1000 genera are being used in indigenous system of medicine which symbolizes the rich tradition for herb and herbal remedies.<sup>1</sup> From the ancient time different cultures around the world have used herbs and plants as a remedy in different diseased condition and maintain health. Many drugs prescribed today in modern medicinal system are derived from plants. Synthetic drug is known for its toxicity which sometimes needs serious medical attention. So in the recent practice of herbalism has got popularity around the globe including the developed countries due to its potency and apparent safety profile.

About 80% of the world population relies on the use of traditional medicine, which is predominantly based on plant material. Scientific studies available on medicinal plants indicate that promising phytochemicals can be developed for many health problems.<sup>2</sup> More over some of the pathological condition where the scientific drugs become crippled but traditional herbal therapy can be a satisfying option which demands an ample amount of research.<sup>3</sup> The attempt is made to present an overview of *Malus domestica* for its phytochemical and pharmacological activities.

*Malus domestica* belongs to family Rosaceae, is a deciduous fruit distributed throughout the world. *Malus domestica* generally called as Apple. Its synonyms are *Apple* (English), *Safarjan* (Gujarati), *Sev* (Hindi, Oriya), *Sebu* (Kannada), *Tsoonth* (Kashmiri), *Safar Chad* (Marathi), *Epal* (Malayalam). Apples are produced commercially in 91 countries on about 13 million acres. World apple production has increased about 17% in the last decade. Average yields are 10,000 lbs/acre worldwide.<sup>4</sup>

### FRUIT

Fruit size typically ranges from 5-9 cm in diameter and available in different colour and it depends on various species

The centre of the fruit contains five carpels arranged in a five point star, each carpel containing 1-3 seeds.



*Malus domestica* fruit

## CHEMICAL CONSTITUENTS

Apple contains a large concentration of flavonoids, as well as a variety of other phytochemicals, and the concentration of these phytochemicals may depend on many factors, such as cultivar of the apple, harvest and storage of the apples, and processing of the apples. Concentration of phytochemicals also varies greatly between the apple peels and the apple flesh.<sup>5</sup>

Apples are freshly fruit with high water content about (85%) and a low sugar content (on average, about 10-12% weight). The main carbohydrates are fructose (6%), glucose (2.2%).

The most well studied antioxidant compounds in the apples are quercetin-3 galactoside, quercetin-3-glucoside, quercetin-3-rhamnoside, catechin, epicatechin, procyanidin, cyanidin-3-galactoside, coumaric acid, chlorogenic acid, gallic acid, and phloridzin.

Recently researchers have examined the average concentrations of the major phenolic compounds in six cultivars of apples. They found that the average phenolic concentrations among the six cultivars were: quercetin glycosides, 13.2 mg/100 g fruit; vitamin C, 12.8 mg/100 g fruit; procyanidin B, 9.35 mg/100 g fruit; chlorogenic acid, 9.02 mg/100 g fruit; epicatechin, 8.65 mg/100 g fruit; and phloretin glycosides, 5.59 mg/100 g fruit.<sup>5</sup>

The compounds most commonly found in apple peels consist of the procyanidins, catechin, epicatechin, chlorogenic acid, phloridzin, and the quercetin conjugates. In the apple flesh, there is some catechin, procyanidin, epicatechin, and phloridzin, but these compounds are found in much lower concentrations than in the peels. Chlorogenic acid tends to be higher in the flesh than in the peel.<sup>6</sup>

Apple peels contain higher antioxidant compound especially quercetin, it has higher antioxidant activity and higher bioavailability than the apple flesh. Apples with the peels were also better able to inhibit cancer cell proliferation when compared to apples without the peels.<sup>6</sup> More recent work has shown that apple peels contain two to six times (depending on the variety) more phenolic compounds than in the flesh, and two to three times more flavonoids in the peels when compared to the flesh.<sup>7</sup>

## THERAPEUTIC USES

"An apple a day keeps doctor away". *Malus domestica* (Apple) a traditional plant widely used since Iron Age and has multiple benefits. Apart from pharmacological screening of

*Malus domestica* edible properties of apples reportedly used for natural therapies as follows.<sup>8</sup>

### ➤ ANTACID

It makes it very suitable to stop stomach acidity due to it contains pectin as well as the influence of the glycine.

### ➤ ANTI-DIARRHEAL AND SOFT LAXATIVE

An apple seems contradictory its high content in pectins turn it into a good regulator of intestinal tract and absorbent value of the pectins make ideal case of colitis, diarrhea, gastroenteritis and in all those cases in that a too abundant and soft defecation is produced.

### ➤ DIURECTIC AND DEPURATIVE

Apple content such as cysteine and arginine as well as the malic acid, it is very appropriate to eliminate the toxins that are stored in the body and besides fighting or preventing the diseases. It recommended in affection like uric acid, gout, urticarial and for the treatment of kidney related diseases.

### ➤ HEARING LOSS

An apple vinegar has very beneficial properties to the health of the ear because it rich in potassium, magnesium zinc and manganese. One of this mineral deficiency can cause deafness.

## PHARMACOLOGICAL ACTIVITIES- AN EVIDENCE BASED APPROACH

### 1. ANT-OXIDANT ACTIVITY

Apple, and especially its peels have been found to have a potent antioxidant activity and can greatly inhibit the growth liver cancer and colon cancer cells. The total antioxidant activity of apples with the peel was approximately 83 $\mu$ mol vitamin-C equivalents, which means that the antioxidant activity of 100 g apples is equivalent to about 1500 mg of vitamin-C. However, the amount of vitamin-C in 100 g of apples is only about 5.7 mg. Vitamin-C is a powerful antioxidant, but this research shows that nearly all of the antioxidant activity from apples comes from a variety of other compounds. Vitamin-C in apples contributed less than 4% of total antioxidant activity.<sup>9</sup>

### 2. ANTI-PROLIFERATIVE ACTIVITY

Apples have been shown to have potent antiproliferative activity in several studies. When Caco-2 colon cancer cells were treated with apple extracts, cell proliferation was inhibited in a dose-dependent manner

reaching a maximum inhibition of 43% at a dose of 50 mg/mL. The same trend was seen in Hep G2 liver cancer cells with maximal inhibition reaching 57% at a dose of 50 mg/mL. Due to its unique combination of phytochemicals in the apples that are responsible for inhibiting the growth of tumor cells.<sup>9</sup> Apples had the third highest antiproliferative activity when compared to eleven other commonly consumed fruits. Apples without peels were significantly less effective in inhibiting Hep G2 cell proliferation when compared to apples with the peel, suggesting that apple peels possess significant antiproliferative activity. It was concluded that apple peels alone inhibited Hep G2 cell proliferation significantly more than whole apples.<sup>10</sup>

### 3. ANTI-MICROBIAL ACTIVITY

Effect of water and alcohol extracts of *M.domestica* fruit was found to be most effective against gram +ve and gram -ve bacteria such as *B.subtilis*, *S.aureus* and *E.coli*, *P.aeruginosa* respectively.<sup>11</sup> According to literature, the antimicrobial activity could be influenced by the phenolic compounds and their polyphenol extracts had stronger inhibition effects on the bacteria. An *in vivo* assay is necessary to confirm the antimicrobial activities of *Malus domestica*, which could be usefully applied to the food, pharmaceuticals, and cosmetics industries. Isolation of the gene responsible for the antimicrobial activity would be an interesting future study topic aimed at identifying the molecule generating the desirable efficacy.

### 4. INHIBITION OF LIPID OXIDATION

It has been found that addition of apple phenolics to human serum decreased diphenylhexatriene-labeled phosphatidylcholine (DPHPC) oxidation in a dose dependent manner. DPHPC is incorporated into low-density lipoprotein (LDL), high-density lipoprotein and very low-density lipoprotein (VLDL) fractions and is an indicator of oxidation. Apple ingestion led to a decrease in DPHPC oxidation, reflecting the apples antioxidant activity *in vivo*. The protective effects of apples on LDL oxidation reached its peak at three hours following apple consumption and returned to baseline levels by 24 hours. Diphenylhexatriene-labeled propionic acid (DPHPA) binds to serum albumin and is a good measure of oxidation within the aqueous phase of human serum. It was also found that consumption of apples also led to a decrease in albumin DHPA oxidation, reaching peak activity at 3 hours.<sup>12</sup>

### 5. ANTI-DEPRESSANT ACTIVITY

Apple ripe with antioxidants and fiber. An apple a day could if eaten with the rest of these foods keep the psychiatrist away, at least for stretches of time. Like berries, apples are high in antioxidants, which can help to prevent and repair oxidation damage and inflammation on the cellular level. Apple juice consumption may increase the production in the brain of the essential neurotransmitter acetylcholine. The researchers found that including apples in your daily diet may protect neuron cells against oxidative stress-induced neurotoxicity.<sup>13</sup>

### 6. CHOLESTEROL LOWERING EFFECT

Effect of *M.domestica* supplementation serum lipids and lipoproteins level in cholesterol-fed male rat showed that supplementation of *M.domestica* reduced the amount of TC, LDL and TG and increased HDL concentration. The effect can be due to antioxidant effect of compounds constituting the food was linked probably by inhibiting lipid peroxidation and decrease production of cholesterol, LDL and triglycerides.<sup>14</sup>

### 7. ANTI-INFLAMMATORY EFFECT

Effect of anti-inflammatory action of apple polyphenol extracts prevents damage to human gastric epithelial cells *in vitro* and to rat gastric mucosa *in vivo*. It was concluded that apple extract reduces gastric erosion in indomethacin (at dose of 35 mg/kg, s.c) induced injury in rats because of phenolic compounds have been shown to exert direct antioxidant effects acting as ROS scavengers, hydrogen donating compounds, singlet oxygen quenchers, and metal ion chelators.<sup>15</sup>

### 8. ASTHMA AND PULMONARY FUNCTION

Apple consumption has been inversely linked with asthma and has also been positively associated with general pulmonary health. It has been found that an apple and pear intake was associated with decreased risk of asthma and a decrease in bronchial hypersensitivity because of it contains high concentration of antioxidant, vitamins, phenolic acid and flavonoids which helping to calm the inflammation in the airway.<sup>16</sup>

### 9. DIABETES AND WEIGHT LOSS

An apple consumption may also be associated with a lower risk for diabetes and its peels was also associated with a decreased risk in type II diabetes due to apple contains in higher concentration of quercetin.

A study was conducted on approximately 400 hypercholesteremic but nonsmoking women were randomized to one of three supplement groups: oat cookies, apples or pears, and each subject consumed one of each supplement three times per day for twelve weeks. The participants who consumed either of the fruits had a significant weight loss after 12 weeks of 1.21 kg, whereas those consuming the oat cookies did not have a significant weight loss. Those consuming fruit also had a significantly lower blood glucose level when compared to those consuming the oat cookies.<sup>17</sup>

### OTHER HEALTH EFFECTS

Recently it has been found that crude extracts from immature apples actually inhibited enzymatic activities of cholera toxin in a dose dependent manner. Additionally, apple extracts reduced cholera toxin induced fluid accumulation in a dose dependent manner. The apple extracts were fractionated and each fraction was tested for inhibitory action on enzymatic activities of cholera toxin. The two apple extract fractions that contained highly polymerized catechins inhibited cholera toxin catalyzed ADP-ribosylation by 95% and 98%. The fraction containing non-catechin polyphenols caused only 3.5% inhibition and the fraction containing monomeric, dimeric, and trimeric catechins caused 39% inhibition.<sup>18</sup>

### CONCLUSION

In the present review, authors have tried to describe active constituents, therapeutic uses and pharmacological activities of *Malus domestica*. It also reveals that *Malus domestica* contains several phytoconstituents and apples contain different vitamins reportedly vitamin A, B and C. Apples have high content of organic acids like malic, citric, tartaric acid, etc. which give the fruit its acid flavour and improve its keeping qualities.

The plant has been studied for its various pharmacological activities like anti-oxidant, antiproliferative, anti-depressant, anti-inflammatory, anti-microbial, inhibition of lipid oxidation and Cholesterol-lowering effect. *Malus domestica* has a great perspective for the treatment of diseases like antacid, anti-diarrheal, soft laxative, diuretic and depurative, hearing loss etc. Further studies and investigations can be performed on the plant for its various pharmacological activities.

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