



## A Review on Pharmacological and Nutritional Benefits of Mango (*Mangifera indica* Linn): A Remedy for Cancer, Diabetes and Gastrointestinal Infections

Fizza Mubarik<sup>1</sup> , Sana Noreen<sup>1</sup> , Fatima Farooq<sup>1</sup> , Ayesha Siddiq<sup>1</sup> , Mudassir Khan<sup>2\*</sup>

<sup>1</sup>University Institute of Diet and Nutritional Sciences, The University of Lahore, Pakistan

<sup>2</sup>Department of Healthcare Biotechnology, Atta-Ur-Rahman School of Applied Biosciences (ASAB), National University of Science and Technology (NUST), Islamabad

### Abstract

Mango is one of the choicest fruits in the world because of its good flavour, attractive colour and fruity fragrance. It belongs to family Anacardiaceae having wide range of varieties and health benefits. It grows in tropical region and has good nutritional profile. Innumerable researches have been done around the world that demonstrated diversified nutritional and pharmacological benefits of *Mangifera indica* Linn. It has particular composition of nutrients and phytochemicals. Different parts of mango trees have different wide ranges of benefits. The flower, seeds, leaves, bark, raw as well as ripe fruits provide extensive variety of pharmacological, medicinal and many health benefits. In addition to the higher values of macronutrients as well as micronutrients, mangoes have a wide range of bioactive compounds present in different portions of plant for example, the primary active constituent present in mango is mangiferin. In this review article we reviewed a number of beneficial characteristics of mango including its antioxidant, anti-diabetic, anti-bacterial, gastric health, anti-cancer and anti-inflammatory activities.

**Keywords:** Mango, mangiferin, anti-diabetic, anti-bacterial, anti-cancer

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**\*Corresponding author:**

Kmudassir71@yahoo.com

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## Contents

1. INTRODUCTION.....	83
2. NUTRITIONAL PROFILE.....	83
3. MICRONUTRIENT COMPOSITION.....	84
3.1 Vitamin .....	85
3.2 Fiber and minerals.....	85
4. PHARMACOLOGICAL BENEFITS OF MANGO .....	85
4.1 Mangiferin .....	85
4.2 Anti-oxidant.....	86
4.3 Anti-diabetic.....	86
4.4 Anti-bacterial .....	87

4.5 Gastroprotective Health.....	87
4.6 Anti-inflammatory.....	87
4.7 Anti-Cancer.....	88
5. CONCLUSIONS.....	88
REFERENCES.....	89

## 1. INTRODUCTION

Mango (*Mangifera indica* Linn) is a tropical fruit which belongs to family Anacardiaceae and having huge range of varieties and health benefits. It has unique composition of nutrients and phytochemicals. Different varieties of mango of around 1365 types exist throughout the world and among them approximately more than 1000 are cultivated and grown in India<sup>1</sup>. Trees of mango have been cultivated and grown in the Indian sub-continent since thousands of years. From the 5<sup>th</sup> and 4<sup>th</sup> centuries BC, mangoes have been grown in Southeast Asia, while around 10<sup>th</sup> century AD, they have been cultivated in West and East Africa. Moreover, mangoes are also cultivated and grown in West Indies, Mexico, Brazil, Caribbean Islands, Southern Europe, and specifically in the coastal and subtropical region of Spain, Portugal and Canary Islands. The most popular specie of mango which is grown in Pakistan and India is known as Alphonso Mango which is exported worldwide. In 2012, statistics of the United Nations stated that the largest producer of mango in the whole world is India (16.2 million tons), however the production of Pakistan, Thailand and China is 2.3, 3.0 and 4.4 million tons respectively<sup>2</sup>.

A wide range of vitamins, polyphenols, antioxidants, carotenoids, and phenolic acids are distributed in different parts accordingly. Mango contains a high nutritional value and being rich in its nutritional and phytochemical composition it exhibits many beneficial characteristics which includes anti-inflammatory, antioxidant, cardiac protection, wound healing, anti-microbial, anti-viral, anti-tumor, anti-pyretic, anti-dysentery, as well as hypolipidemic, immunomodulatory, gastroprotective and hepatoprotective effects<sup>3-6</sup>.

Due to its exotic flavor, sweet taste and numerous health benefits, mango is commonly known as the “King of Fruits”. Mango flesh is consumed in both unripe as well as ripe forms. Mostly fresh mangoes are eaten but a wide variety of beverages and processed foods can also be prepared from mangoes. These may include pickles, chutneys, vinegar, beverages as well as desserts, meat tenderizer and even dessert flavorings. Along with an increase in the trade of fresh mangoes, there is also a massive increase in the trade of processed foods prepared from mangoes throughout the world<sup>7</sup>.

In addition to the higher values of macronutrients as well as micronutrients, mangoes have a wide range of bioactive compounds present in different portion of its plant for example, mangiferin, which is the primary active constituent present in mango. The main aim of the following review article is to deliver an assessment of the nutritional value of mango, its bioactive compounds along with their beneficial effects in different disease conditions.

## 2. NUTRITIONAL PROFILE

Mango fruit contains both macronutrients as well as micronutrients which enhance the nutritional value of this fruit. The macronutrient composition of mango flesh varies a little among different varieties of mango fruit. To evaluate the macronutrient composition of mango kernel flour (variety Ikanekpo, Nigeria), a research was carried out, which concluded the macronutrient composition per kilogram as: 500g starch, 94g fat, 66.1g protein and 28g fiber. The approximate percentage of fat contents of mango kernel ranges from 6-12% depending upon dry matter, however fatty acid profile presented high levels of oleic acid and stearic acid<sup>8</sup>. European Union Authorities has approved Mango seed fat as a substitute for cocoa butter.

The protein content of mango seed kernel is usually low but it contains essential amino acids which show the presence of good quality protein. However, it has been also seen that pattern among limiting amino acids such as cysteine, valine, methionine and isoleucine varies among different cultivars. The studies on assessment of macronutrient composition of Egyptian mango seed kernel having varieties including Balady,

Zebda and Succary presented that the amount of essential amino acids present in mango seed kernel is higher than the reference protein values of Food and Agriculture Organization (FAO)<sup>9</sup>.

Mango contains adequate amounts of fiber which is beneficial for numerous gastrointestinal diseases. The communities among many developing countries that do consume more amounts of fiber have been shown to have lower percentage of GI diseases. Dietary fiber has many healthy effects on the gut<sup>10</sup> and overall health of human beings and other body functions because dietary fiber is also associated with decreased incidence of diseases including obesity, cancer, diabetes, chronic bowel disorder and cardiovascular diseases<sup>11</sup>.

Keitt mango, being cultivated and grown in Florida in both unripe and ripe states, contains the total dietary fiber content as 1.4g and 1.6g in every 100g fruit respectively. However, pectin is present in a large portion<sup>12</sup>. The mineral content is high in the fiber obtained from mango peel of Haden mango including zinc (32.5 mg/kg), magnesium (950 mg/kg), calcium (4445 mg/kg), iron (175 mg/kg) and potassium (2910 mg/kg) which are required for the good health of humans. The carotenoids, provitamin A carotenoids along with  $\beta$ -carotene are present in abundance in the mango flesh in many mango varieties<sup>13,14</sup>.

Moreover, mango flesh also contains dehydroascorbic acid and ascorbic acids. Hence, this fruit can prove to be a good source of vitamin C which has many benefits for human health. Therefore, the consumption of mango fruit daily can make the population able to fulfill their recommended dietary requirements of Vitamin C and Vitamin A in combination with other macro and micro-nutrients along with a variety of phenolic compounds and dietary fiber. Table 1 presents the nutrient composition of mango fruit.

**Table 1.** Nutrient composition of Mango Fruit per 100 g (3.5 oz)<sup>15</sup>.

Nutrients	Quantity	DV%	Nutrients	Quantity	DV%
Fat	0.4 g	1%	Saturated Fat	0.1 g	1%
Carbohydrates	28.1 g	9%	Vitamin K	6.9 $\mu$ g	9%
Sugars	24.4 g	27%	Vitamin E	1.8 mg	9%
Protein	0.82 g	2%	Vitamin C	45.7 mg	76%
Calcium	16.5 mg	2%	Thiamine (Vit. B1)	0.1 mg	6%
Phosphorus	18.2 mg	2%	Riboflavin (Vit. B2)	0.1 mg	6%
Magnesium	14.8 mg	4%	Vitamin B6	0.119 mg	9%
Potassium	257 mg	7%	Vitamin B12	120 $\mu$ g	0%
Copper	0.2 mg	9%	Pantothenic acid (Vit. B5)	0.3 mg	3%
Sodium	3.3 mg	0%	Niacin (Vit. B3)	1.0 mg	5%
Zinc	0.1 mg	0%	Folate (Vit. B9)	43 $\mu$ g	11%
Selenium	1.0 $\mu$ g	1%	Choline	12.5 mg	<2%
Iron	0.2 mg	1%	Dietary Fiber	3.0 g	12%
Manganese	0.0 mg	2%	Energy	448 KJ	5%

\*DV= Dietary Value

### 3. MICRONUTRIENT COMPOSITION

Innumerable food components and nutrients are responsible for the maintenance of normal functioning of human body. Phytonutrients present in foods play the role of health enhancers and also acts as protective measure for a number of specific diseases. Mango is a popular fruit because of its differential flavor and nutritional worth. (Figure 1) It is considered as a rich source of different vitamins such as A, B and C. Along with vitamins, minerals that are present are calcium, sodium, potassium, magnesium, iron and phosphorous. Other constituents in little amount that are present in a mango are malic, citric and tartaric acid<sup>16</sup>.

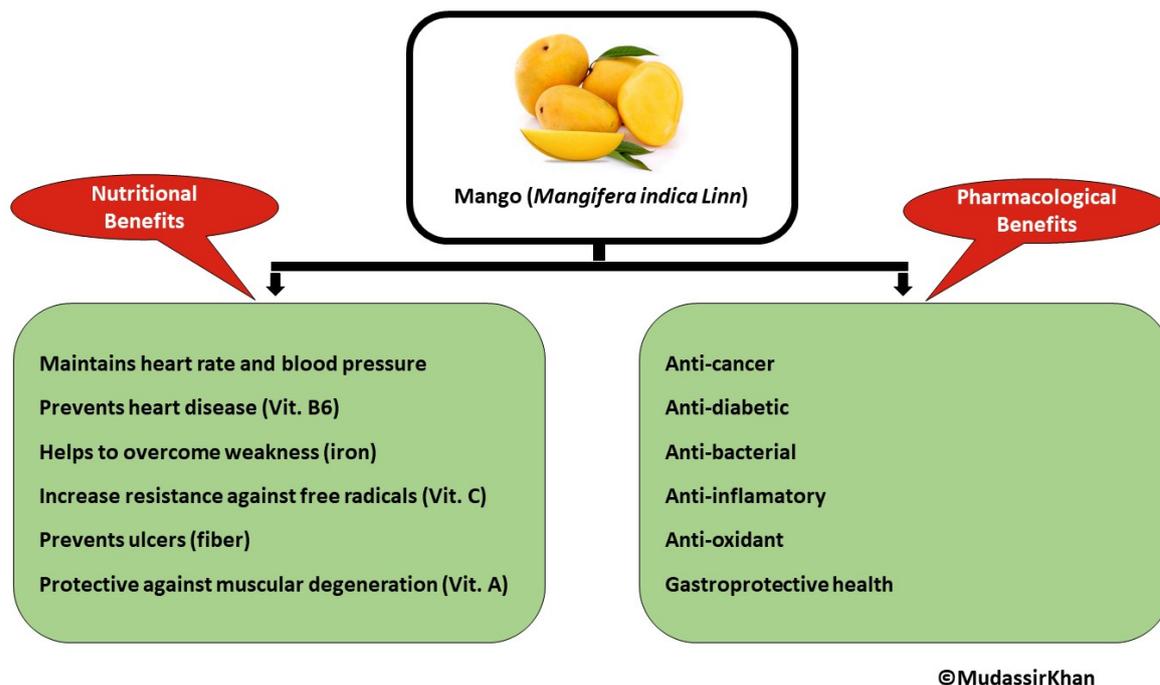


Fig. 1. Health Benefits of Mango

### 3.1 Vitamin

Vitamin A is present in mango which is integral for vision as well as provides protection against muscular degeneration. Blood circulation in skin and mucus membrane becomes efficient in existence of vitamin A. Mango is also high source of vitamin B6, also called as pyridoxine. Blood vessel linings can be damaged by an amino acid present in the blood, known as homocysteine. Pyridoxine has the power to lower the levels of homocysteine, which as a result helps in prevention of heart diseases<sup>17</sup>. Vitamin C is abundantly present in both unripe and ripe mango. It has been observed to decrease cholesterol level that is LDL in the body<sup>18</sup>. Other vitamins that are present in minute quantities in mango include vitamin E, vitamin K, thiamin, riboflavin, folate, niacin, and pantothenic acid<sup>19</sup> (Table 1). Intake of mango also enhances resistance against free radicals and other infectious agents<sup>20</sup>.

### 3.2 Fiber and minerals

Fiber helps in catabolism of protein during the process of digestion. It can be abundantly found in a mango. The prebiotic fiber prevents disorders such as irritable bowel syndrome or ulcers and this is done as the fiber helps the growth and maintenance of healthy bacteria in the gut<sup>21</sup>. As mango is high source of iron it is beneficial for people who are anemic. Menopause causes weakness in females which can be overcome by maintaining iron requirements by intake of mangoes. Fresh mangoes contain increased amount of potassium which is an integral element required by cells and is a part of body fluids that play a major role in maintenance of heart rate and blood pressure<sup>22</sup>. Mangoes protect the body from damage caused by free radicals as it contains phytochemicals such as beta carotene, astragaloside and quercetin<sup>23</sup>.

## 4. PHARMACOLOGICAL BENEFITS OF MANGO

### 4.1 Mangiferin

It is a compound present in the fruit, leaves, bark and roots of mango<sup>5</sup>. Mangiferin, is a crystalline powder in nature that is light yellow in colour, has slight solubility in ethanol, sparing solubility in water and ethanol whereas it is insoluble in acetone, diethyl ether and n-hexane<sup>24</sup>. Mangiferin possesses a number of

beneficial characteristics including its antioxidant activity, its role in pro-hypoglycemic activity, maintenance of cholesterol levels and inhibition of TNF $\alpha$  expression.

#### 4.2 Anti-oxidant

The functionality and structure of biological molecules such as DNA, protein and lipids can be altered by oxidation caused by reactive oxygen species (ROS). To prevent this and also occurrence of several chronic diseases a number of antioxidants are beneficial including vitamin C and E, beta carotene. The antioxidant defense helps in treatment of chronic disorders as well as provides chemoprevention. In a research done by Saha et al. it was observed that mangiferin possesses the ability of scavenging radicals due to presence of hydroxyl groups and C-glucosyl linkage<sup>25</sup>.

In another study hydrogen peroxide-induced lipid peroxidation in human peripheral blood lymphocytes was dramatically reduced in a process depending upon dose<sup>5</sup>. Mangiferin is a potential iron chelator that has the ability to protect from UV radiations and hydroxyl radicals. In a research study by Pardo-Andreu et al. mangiferin was observed to show the activity of counterbalancing oxygen free radical formation which was caused by iron and toxicity caused by it<sup>26</sup>.

The protecting nature of mangiferin was analyzed in an experiment against oxidative injury caused by hydrogen peroxide and cell death in cultured cells MC3T3-E1. It was observed that mangiferin prevented the cells from oxidative stress by ERK5/Nrf2 signaling modulation. This property helps to consider it a possible therapy for osteoporotic patients<sup>27</sup>.

Pokorski et al. explained the hepatoprotective property of mangiferin against hepatic injury caused by CCl<sub>4</sub><sup>24,28</sup>. In another independent study mangiferin protected hepatic tissues against oxidative stress induced by arsenic<sup>29</sup>.

#### 4.3 Anti-diabetic

A number of investigations have been done to analyze potential of mangiferin against diabetic. Mangiferin plays a role in glucose metabolism regulation and insulin resistance. In a research study it was observed that mangiferin treatment of 8 weeks drastically lowered plasma glucose and level of triglycerides in mice prone to diabetes. Increased pancreatic beta cell mass was observed as well as enhanced uptake of glucose and insulin by increased phosphorylation of AMP which is activated protein kinase<sup>30</sup>.

Mangiferin treatment can prevent renal fibrosis and decrease collagen IV. Collagen IV is the most important structural collagen (protein) as it forms the backbone of the basement membrane. It lies under the epithelial and endothelial cells forming a network and also acts as a barrier in between tissue compartments. It is a network-forming collagen that underlies epithelial and endothelial cells and functions as a barrier between tissue compartments<sup>31</sup>. It has been observed further to reduce IL-1 $\beta$  among kidneys of diabetic rats. The investigation resulted that treatment of 15, 30 and 60 mg/kg body weight with mangiferin for a time period of 9 weeks decreased kidney weight and reduced renal issues, also helped in normalizing blood urea nitrogen<sup>32</sup>.

According to the present state of economy we know that diabetes treatment treating diabetes can put a burden on health as well as financial conditions. This can be overcome by trying to implement the use of mangiferin for its therapeutic benefits. It has been observed that diets that are based on plants help efficiently to decrease blood sugar levels and possibly eradicate the use of traditional medicines as therapy. Doing so also helps in elimination of possible side effects. Dr. Roy Chowdhury conducted a clinical trial in which he observed that blood glucose level decreased as well as reduced glycemic index was observed in about 84% of patients who were consuming a strict vegetarian diet including raw mango fruit. The researchers also analyzed that warm water extract of whole leaves of mango or in the form of powder portrayed beneficial effects in diabetics<sup>33</sup>.

#### 4.4 Anti-bacterial

In a research study significant activity of mango stems and leaves extract has been observed against a number of bacteria such as *Streptococcus pyogenes*, *Staphylococcus aureus*, *Streptococcus pneumonia*, *Candida albicans*, *Pseudomonas aeruginosa*, *Enterococcus faecalis*<sup>34</sup>. The activity was also observed against other bacteria such as *E. coli*, *Listeria monocytogenes* and *Salmonella*<sup>35</sup>. Antibacterial activity of mango extract was also observed against gram negative and positive bacteria, it is thought to be due to existence of mangiferin and gallotannin in the extract<sup>36</sup>.

#### 4.5 Gastroprotective Health

Mangiferin transits through the GI tract and metabolized into various phenolic acid derivatives including 3,4-dihydroxy-phenylacetic acid, 3,4-dihydroxybenzoic acid, 3,4,5-trihydroxybenzoic acid, 2,4,6-trihydroxybenzoic acid, and the mangiferin aglycone 1,3,6,7-tetrahydroxyxanthen-9-one, by colonic intestinal microflora and imparts medicinal benefits<sup>37</sup>. A number of investigations have resulted in the analysis that inflammation in intestine and impaired motility of gastrointestinal tract can be reduced effectively by mangiferin<sup>38</sup>.

Myeloperoxidase activity, adhesion molecules, nitrate levels and cytokines were significantly suppressed by use of mangiferin. Based on these investigations and results mangiferin was considered to possess therapeutic potential against inflammatory bowel diseases<sup>38</sup>. In a study it was observed that mangiferin exhibited gastroprotective activity against ulcer, gastric lesion induced by ethanol and endomethacin, as well as gastric mucosal non-protein sulfhydryl depletion in mice<sup>39</sup>.

In a research study carried out by Kakino et al. mangiferin was shown to exhibit laxative property through acetylcholine receptors and increased regularity of GI tract in a sample of mouse having constipation<sup>40</sup>. Another investigation carried out by Somani et al. showed that through the process of eliminating oxidative stress and inflammation by modulation of MMP-9 and TNF- $\alpha$  mangiferin can decrease the colonic injury, this study provided the evidence that mangiferin which is present in mango can potentially treat IBD<sup>41</sup>.

Another significant benefit of mangiferin was observed that it can significantly eradicate *H. pylori* bacteria and prevent GI inflammation and gastric cancer. Mangiferin inhibited the inflammatory markers such as TNF $\alpha$ , NF- $\kappa$ B subunit, IL-1 $\beta$ , p65 and IL-8, as well as with the help of inflammatory response deactivated NF-p65<sup>42</sup>. Thus, a diet enriched in mangiferin that is plant based or in the form of supplements can be beneficial for gastroprotective health.

#### 4.6 Anti-inflammatory

Several numbers of studies have been done to show the phytochemical property of mango which aids to play the anti-inflammatory role in different diseases related with inflammatory responses<sup>43,44</sup>. Some common disorders characterized by chronic inflammation include IBD (inflammatory bowel disease), ulcerative colitis etc. These disorders also contribute towards mucosal damage in large intestine. Colon and rectal cancers are the high risk diseases linked with this inflammation<sup>45</sup>. The mucosa of patients with such diseases has been shown to form increased amount of pro-inflammatory cytokines e.g. IL-1, IL-12, IL-6, and TNF- $\alpha$ <sup>46,47</sup>. A transcriptional factor known as kappa-B (NF- $\kappa$ B) is responsible for the regulation of expression of pro-inflammatory cytokines, the levels of which has been already found to be elevated in the mucosa of IBD patients<sup>48</sup>. Mango extracts have been found to play anti-inflammatory role in the sample of murine with ulcerative colitis in an experiment. It was seen that the ulcerative colitis symptoms like diarrhea, weight loss and colon shortening were reduced when the aqueous solution with the extract from the bark of *Mangifera indica* (mango) was used. Also, the mango extract decreased the expression of pro-inflammatory cytokines like iNOS, COX-2, TNF- $\alpha$ , and TNFR-2 in the tissues of colon<sup>49</sup>.

The anti-inflammatory property of *Mangifera indica* has also been proven in liver and cardiac protection in several researches<sup>50,51</sup>. The extracts of mango provide protection against Lipopolysaccharide (LPS) and D-galactosamine induced acute liver inflammation. In a dose-dependent experiment, mangiferin was seen to regulate the expression of pro-inflammatory cytokines Nrf2 and HO-1. Mangiferin also reduced the liver NLRP3 induced by LPS and D-galactosamine.<sup>52</sup> It was stated by the researchers that mangiferin also plays a

vital role in defense against hepatic inflammation through the process of activating the Nrf2 pathway as well as maintaining the regulation of inflammasome activity of NLRP3.<sup>26</sup> The ethanol extract of *Mangifera Indica L.* leaf enriched in mangiferin was shown to have anti-inflammatory activity in cardiac protection<sup>26</sup>.

#### 4.7 Anti-Cancer

The anti-cancer activity of mango has been shown due to the presence of different bioactive compounds presents in different parts of *Mangifera indica*. In pancreatic cancer, the methanol extract of mango was used, which due to the isolated bioactive compounds like mangiferolate and isoambolic acid in mango extract, produced cytotoxic effects<sup>53</sup>. Moreover, it was reported that an aqueous solution mango mesocarp produced anti-cancer activity in colon and carcinoma cancer cells in humans as well as in colorectal cancer in rodent sample<sup>54</sup>. Mango polyphenolics and kernel has effect on induction of apoptosis of breast cancer cell lines, also polyphenol decreased cell proliferation, Metallic nanoparticles have antimicrobial and anticancer activities, silver nanoparticles have antiproliferative and apoptosis-inducing properties, plants extracts can be used efficiently in its synthesis<sup>55</sup>. The ethanolic extract of seed of mango is responsible to promote cell death in both oestrogen-positive and -negative breast cancer and not in normal breast cells, it has anticancer activities like that of Buckwheat<sup>55,56,57</sup>. In oestrogen-negative breast tumour cells, the production of ROS which enhances cell death through Bax activation and cytochrome c release has been related to the cytotoxic effect of mango seed extract. It has also been shown that gallotannin and gallic acid-rich mango extracts are responsible for the antitumor effects in BT474 breast cancer cells as well as athymic mice bearing BT474 cells as xenografts through interruption of the PI3K/Akt/mTOR pathway<sup>58</sup>.

## 5. CONCLUSIONS

Plants are vital sources of medicines from ancient times as they have the ability to boost health and cope up with weaknesses and body requirements. All parts of different various plants possess nutrients and metabolites that have great importance therapeutically. There has been a rise in plant extract use for this purpose. One of such therapeutically important plant is Mango the king of fruits. The present review has led to the results that nutrients and phytochemicals present in mango are beneficial in counteracting pro-inflammatory molecules, pathologies such as cancer, inflammatory reactions, maintenance of gastroprotective health, as well as help fight diabetes. Besides pharmacological benefits mango has also been seen to provide vital nutritional benefits to human health including overcoming weakness, maintaining vision, helping in digestion, and controlling heart rate and blood pressure.

## CONFLICT OF INTEREST

All authors declare no conflict of interest regarding this article.

Akt	Protein kinase B
AMP	Adenosine monophosphate
BT474	Breast tumor cell line
CCl4	Carbon tetrachloride
COX-2	Cyclooxygenase-2
DNA	Deoxyribonucleic acid
ERK5	Extracellular-signal-regulated kinase 5
FAO	Food and Agriculture Organization
HO-1	Heme Oxygenase 1
IBD	Inflammatory bowel disease
IL-1	Interleukin-1
IL-6	Interleukin-6
IL-8	Interleukin-8
IL-12	Interleukin-12
IL-1 $\beta$	Interleukin 1 beta

iNOS	Inducible nitric oxide synthase
LPS	Lipopolysaccharide
MC3T3-E1	Osteoblast precursor cell line derived from <i>Mus musculus</i> (mouse) calvaria
MMP-9	Matrix metalloproteinase 9
mTOR	Mammalian target of rapamycin
NF- $\kappa$ B	Nuclear factor kappa-light-chain-enhancer of activated B cells
NLRP3	Nucleotide-Binding Domain, Leucine-Rich Containing Family, Pyrin Domain Containing-3
Nrf2	Nuclear factor erythroid 2-related factor 2
PI3K	Phosphatidylinositol-3-kinase
ROS	Reactive oxygen species
TNF $\alpha$	Tumor necrosis factor alpha
TNFR-2	Tumor necrosis factor receptor 2
UV	Ultra violet

### ORCID

Fizza Mubarik	 <a href="https://orcid.org/0000-0002-5161-2539">https://orcid.org/0000-0002-5161-2539</a>
Sana Noreen	 <a href="https://orcid.org/0000-0002-4040-5454">https://orcid.org/0000-0002-4040-5454</a>
Fatima Farooq	 <a href="https://orcid.org/0000-0002-3529-071X">https://orcid.org/0000-0002-3529-071X</a>
Ayesha Siddiq	 <a href="https://orcid.org/0000-0003-2507-5503">https://orcid.org/0000-0003-2507-5503</a>
Mudassir Khan	 <a href="https://orcid.org/0000-0002-8184-3557">https://orcid.org/0000-0002-8184-3557</a>

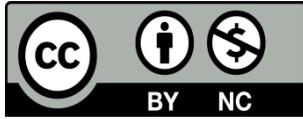
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