Vol. 4 No. 3 (2025)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

THERAPEUTIC INSIGHTS INTO THE LIPID LOWERING AND ANTIOXIDANT ACTIONS OF CURCUMA LONGA

Muhammad Mudassar
College of Allied Health Professionals, Faculty of medical sciences, Government College University Faisalabad, Pakistan
Amna Kausar
College of Allied Health Professionals, Faculty of medical sciences, Government College University Faisalabad, Pakistan
Muhammad Mahboob Sajid
Institute of Microbiology, Government College University Faisalabad, Pakistan
Husnain Khalid
Department of Microbiology, Government College University Faisalabad, Pakistam
Saad Ullah Sani
College of Allied Health Professionals Government College University Faisalabad, Pakistan
Rabia Anum
Institute of Business Management, Karachi Pakistan
Rimsha Zainab
Department of Botany, Shaheed Benazir Bhutto Women University, Peshawar, Pakistan
Shafqat Rasool
School of Eastern Medicine, Minhaj University Lahore, Pakistan
Iftikhar Younis Mallhi
School of Human Nutrition and Dietetics, Minhaj University Lahore, Pakistan
Fethi Ahmet Ozdemir
Department of Molecular Biology and Genetics, Faculty of Science and Art, Bingol University, Bingol, 12000, Türkiye
Gawel Solowski
Department of Molecular Biology and Genetics, Faculty of Science and Art, Bingol University, Bingol, 12000, Türkiye
Muhammad Akram
Department of Eastern Medicine, Government College University Faisalabad Pakistan
Corresponding Author: muhammadakram@gcuf.edu.pk

Vol. 4 No. 3 (2025)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Author Details

Keywords:

Hyperlipidemia, Free Radicals, Anti-Hyperlipidemia, Anti-Oxidant, Curcumin

Received on 03 Aug, 2024

Accepted on 02 Sept 2025

Published on 04 Sept 2025

Corresponding E-mails & Authors*:

Muhammad Akram

muhammadakram@gcuf.edu.pk

Abstract

Curcuma longa, commonly known as turmeric and belonging to the Zingiberaceae family, has been utilized in Asian countries for decades not only as a flavor or spice but also for medicinal purposes. Numerous experiments conducted on animals and humans have demonstrated its miraculous effects in treating various diseases. Extensive research has proven that turmeric possesses significant potential to prevent or cure certain diseases due to its antiviral, antibacterial, antioxidant, antitumor, antifungal, anti-flatulent, anti-inflammatory, anticancer, antidiabetic, hepatoprotective, cardioprotective, anti-allergic, anticoagulant, and immunity-boosting properties. As the trend towards herbal medicines continues to grow, with people increasingly opting for traditional herbal products for the prevention and treatment of their ailments, researchers, research organizations, and pharmaceutical industries are actively exploring the non-revealed pharmacological uses of various herbs. Turmeric is available in various forms, such as tablets, capsules, creams, and ointments, and is consumed not only in underdeveloped countries but also in industrialized nations. This literature review aims to shed light on the antioxidant and anti-hyperlipidemic effects of ***Curcuma longa***.

CURCUMA LONGA/CURCUMIN

The herbal medicine industry is rapidly growing as an alternative to conventional medicines. Many active ingredients in manufactured preparations are derived from plant compounds, offering a wide range of therapeutic uses. Herbal products are gaining popularity due to concerns about the environmental impact of artificial medications and the increasing resistance of parasites to toxic chemicals (Magi &Sahk, 2003). Turmeric, or *Curcuma longa*, is an evergreen herb belonging to the *Zingiberaceae* family, widely cultivated in Asia, particularly in India and China. The rootstock, which is the medicinal part of the plant, produces a yellow powder. Desiccated Curcuma longa is the source of

turmeric, providing curry powder with its characteristic yellow color. It is known by various names, such as Curcum in Arab states, Haridra (Sanskrit, Ayurvedic), Indian saffron, Kyoo or Ukon (Japanese), and Jianghuang (yellow ginger in Chinese) (Goel et al., 2008). Curcuma Longa is a traditional food ingredient, and its primary active component, curcumin, belongs to the curcuminoid family. The root stock, a subterranean stem that is wide and fleshy, supports mature leaves and is a part of turmeric with potential medicinal properties. The therapeutic benefits of curcumin can be attributed to the presence of bioactive compounds called curcuminoids. Curcumin, one of the most remarkable curcuminoid components, tends to dissolve in fat and is a polyphenolic compound with a small molecular weight, making it insoluble in water and ether but soluble in dimethylsulfoxide, ethanol, and other natural solvents (Aggarwal et al., 2003).). Curcumin is stable at the acidic pH of the stomach (Kharat et al., 2017). Other components present in turmeric include volatile oils such as atlantone, zingiberone, and turmerone, proteins, sugars, and resins (Pawar et al., 2014). The active component of curcumin is isolated from the plant of Curcuma Longa, which imparts its characteristic yellow color. In French, it is also known as terre merite, and in many languages, it is referred to as "yellow root." In Arabic, it is called Kurkum or Uqdah safra. Curcuma Longa has at least 53 unusual names in Sanskrit (Kant et al., 2014).

Curcuma Longa has been consumed as traditional herbal medicine due to its diverse benefits, such as anti-inflammatory (Gomez et al., 2017), antimicrobial (Prasad et al., 2014), antioxidant (Rheim et al., 2015), antimutagenic (Noorafshan et al., 2013), and various therapeutic properties (Gupta et al., 2013). Curcumin undergoes rapid metabolism, limited absorption, and rapid elimination. Several agents have been developed to enhance curcumin's bioavailability. One of the most promising is piperine,

which improves curcumin's bioavailability by blocking its metabolic pathway (Hu et al., 2015). Piperine enhances curcumin's bioavailability by up to 2000% (Rungseesantivanon et al., 2010). Curcuminoids are available in various dosage forms, including ointments, capsules, and tablets (Chuengsamarn et al., 2012).

Curcuminoids have been recognized by the United States Food and Drug Administration as Generally Recognized as Safe (Akbik et al., 2014). Rhizomes are cooked until they reach a temperature where they release vapors, after which they are desiccated and ground to produce the distinctively intense yellow spice. Turmeric powder has a spicy bitter flavor and a gentle fragrance reminiscent of ginger and orange. While turmeric powder is best known as a key ingredient in curry seasoning, it also provides mustard its intense yellow color. Beyond its use in cooking, turmeric has been consumed extensively in traditional medicinal products in Pakistan, India, and Bangladesh due to its numerous valuable properties (Chattopadhyay et al., 2004). Turmeric is a plant distributed throughout tropical and subtropical regions of the world, primarily cultivated in Asian countries such as China and India. The plant grows up to 1 m tall with a short stem. Turmeric is a globally important spice with widespread human consumption, particularly among Eastern populations (Ravindran et al., 2007). Apart from its use as a spice, it is employed as traditional medicine in Asian countries like India, Bangladesh, and Pakistan due to its beneficial properties (Chattopadhyay et al., 2004). It is known as turmeric (Zarchooveh in Iran) and has been used for its flavoring and medicinal properties (Govindarajan et al., 1980). Contemporary traditional medicinal products claim its powder's efficacy against gastrointestinal diseases, particularly for biliary and hepatic disorders, diabetic wounds, rheumatism, inflammation, sinusitis, anorexia, coryza, and cough (Ammon et al., 1992). Modern studies have validated

turmeric's anti-diabetic, antioxidant, hypolipidemic, anticancer, hepatoprotective, anti-inflammatory, anticoagulant, antimicrobial, anti-venom, nephroprotective, and anti-human immunodeficiency virus activities, making it a condiment with multifaceted therapeutic properties..

THERAPEUTIC USE OF *CURCUMA LONGA*

Curcumin administration results in significant reductions in circulating lipoprotein concentrations, subsequently modulating total cholesterol levels and hepatic lipid metabolism. Concomitantly, curcumin treatment elevates hepatic α-tocopherol concentrations, suggesting synergistic interactions between curcumin and vitamin E that may enhance tocopherol bioavailability while promoting cholesterol homeostasis.The antioxidant mechanisms of curcumin involve complexation with phosphatidylcholine and lecithin components, facilitating chelation of divalent metal ions that contribute to oxidative stress pathways. Curcumin pretreatment significantly attenuates experimentally-induced hepatotoxicity while elevating arachidonic acid levels in a dose-dependent manner (Bagchi, 2012). Curcumin demonstrates gastroprotective activity against phenylbutazone-induced ulceration in guinea pig models at doses of 50 mg/kg (Yadav et al., 2013). Both in vitro and in vivo investigations in rodent models have established curcumin's carminative properties. Additionally, sodium curcuminate exhibits antispasmodic activity in guinea pig ileal preparations, indicating smooth muscle relaxant effects (Jamil et al., 2018).Turmeric exhibits significant wound healing acceleration through the promotion of tissue regeneration processes (Bai et al., 2024). Topical curcumin application at injury sites enhances healing kinetics through multiple mechanisms including anti-inflammatory activity and cellular proliferation enhancement. These findings support the therapeutic utility of *Curcuma longa* across diverse

pharmaceutical formulations for managing various pathological conditions, including post-surgical wound management. (Parveen *et al.,* 2017).

CHEMICAL CONSTITUENTS OF *CURCUMA LONGA* (TURMERIC)

Among the various compounds isolated from turmeric, bisdemethoxy and demethoxy derivatives are also present. Curcumin has a melting point between 176–177 °C and can form a salt with a reddish-brown colour when reacted with alkali. Curcumin is soluble in ethanol, alkali, ketones, acetic acid, and chloroform (Chattopadhyay et al., 2004). Turmeric contains 6.3% protein, 69.4% carbohydrates, 5.1% fat, 13.1% moisture, and 3.5% minerals. The essential oil of turmeric, obtained through steam distillation, contains 5.8% zingiberene (25%), sesquiterpenes (53%), cineol (1%), sabinene (0.6%), borneol (0.5%), and α-phellandrene (1%). Curcumin, responsible for the yellow coloration of turmeric, constitutes 3–4% of its composition, consisting of 94% curcumin I, 6% curcumin II, and 0.3% curcumin III (Ammon et al., 1991)).

HYPERLIPIDEMIA

Hyperlipidemia, a modifiable risk factor for the deposition of fatty material on the inner walls of arteries (atherosclerosis) and associated cardiovascular diseases, including renal failure, coronary heart disease, myocardial infarction, and cerebral stroke, has become a significant global health concern in recent years (Xu et al., 2014). Hyperlipidemia is a diverse group of diseases characterized by elevated lipid levels in the bloodstream, including phospholipids, triglycerides, cholesterol, and cholesterol esters. The term "hyperlipidemia" refers to increased concentrations of lipids, either cholesterol, triglycerides, or both, in the bloodstream. Elevated triglyceride levels in the blood are termed hypertriglyceridemia, while increased cholesterol levels are referred to as hypercholesterolemia (Watson et al., 1993; Ford et al., 1996; Johnson et al., 2005).

Another associated condition, dyslipidemia, signifies a disorder in lipoprotein metabolism, including deficiency or overproduction of lipoproteins. These disorders may manifest as elevated serum triglyceride concentrations, low-density lipoprotein (LDL), total cholesterol, and decreased high-density lipoprotein (HDL) levels. The primary objective in managing hyperlipidemia is to minimize the risk of developing cardiovascular, cerebrovascular, and ischemic heart diseases. Cholesterol is the primary unsaturated steroid alcohol found in animal tissues, with dietary intake being the main source. However, it can also be synthesized within the body by other tissues and the liver. Cholesterol is absorbed from the intestine and transported to the liver via chylomicron remnants. Hepatic cholesterol enters the circulation as very low-density lipoprotein (VLDL), which is metabolized by lipoprotein lipase to intermediate-density lipoprotein and LDL. LDL is then released by hepatic or peripheral tissues. Cholesterol plays a crucial role in essential metabolic pathways, such as steroid hormone synthesis, vitamin D metabolism, and bile acid metabolism. Elevated dietary cholesterol levels are observed as a significant factor in the development of ischemic heart disease, with the focus being primarily on general and coronary vascular outcomes of hyperlipidemia. Hyperlipidemia is characterized by an increasing concentration of fats in the bloodstream. LDL promotes the deposition of free fatty acids in arteries, leading to an increased risk of coronary heart disease. In contrast, HDL has an anti-atherogenic effect, and low HDL levels also enhance the risk of coronary heart disease. High lipid content in the blood is one of the significant factors linked to atherosclerosis, alongside other risk factors such as smoking, hypertension, and diabetes mellitus. Atherosclerosis, hyperlipidemia, and associated cardiovascular diseases have become a major global health issue in recent years (Karam et al., 2015). Hyperlipidemia has been recognized as

a modifiable risk factor for cardiovascular disease, the most widespread cause of death worldwide, accounting for approximately 17 million fatalities annually (Mith et al., 2004). There are two most important categories **of** hyperlipidemia:

Primary Hyperlipidemia: This may occur due to excessive food intake that is rich in fats and cholesterol or several hereditary factors and genetic defects

Secondary Hyperlipidemia: Hyperlipidemia can occur due to various ailments or metabolic disruptions, such as obstructive liver disease, hypothyroidism, and diabetes mellitus. These underlying causes are the most frequent pathological type of hyperlipidemia in dogs (Xenoulis et al., 2010; Nelson et al., 2004). A range of diseases have been implicated in causing hyperlipidemia. Endocrine disorders are the most common cause of canine hyperlipidemia, resulting from endocrine diseases such as hyperadrenocorticism, diabetes mellitus, or hypothyroidism (Whitney et al., 1992; Bauer et al., 2004; Rogers et al., 1977; Rogers et al., 1975; Feldman et al., 2014; Peterson et al., 1988). Increased serum cholesterol and triglyceride concentrations have been reported in dogs with hypothyroidism (Xenoulis et al., 2010; Barrie et al., 1993; Dixon et al., 1999; Panciera et al., 1994; Wilson et al., 1986).

MANAGEMENT OF HYPERLIPIDEMIA

The treatment strategies for hyperlipidemia aim to reduce lipid levels in the blood. Numerous chemical preparations are available to lower cholesterol levels, commonly known as lipid-lowering drugs, such as fibrates, statins, nicotinic acid, and ezetimibe. However, many of these drugs are expensive and have unwanted side effects (Thomas et al., 2003). The primary objective in managing hyperlipidemia in patients is to reduce the risk of developing cardiovascular, cerebrovascular, and ischemic heart diseases. To address high lipid levels and manage hyperlipidemia in humans, various interventions

have been implemented, including exercise, dietary control, and the administration of lipid-lowering drugs (Stone et al., 1996). The most essential drugs for dyslipidemia management are undoubtedly statins, which reduce cholesterol by inhibiting the biosynthetic pathway of cholesterol. The liver is their primary site of action, where they inhibit β-Hydroxy β-Methylglutaryl CoA reductase (HMG-CoA reductase), the metabolic pathway responsible for producing isoprenoids and cholesterol. Statins have been demonstrated in numerous clinical studies to decrease cardiovascular incidents and mortality. Statins effectively lower low-density lipoprotein (LDL) levels, reducing both mortality and morbidity associated with coronary heart disease by nearly 30%. Statin therapy is also recommended for prevention in all patients with identified cardiovascular disease. High-dose statins should be initiated in patients with acute coronary heart syndrome (Wang et al., 2006). The USA, UK, and Canadian practice guidelines are available to assist healthcare professionals in managing hyperlipidemia. These guidelines emphasize that lifestyle modifications are the foundation of hyperlipidemia management, with LDL cholesterol being the primary target of treatment. Treatment of hyperlipidemia is beneficial for patients with identified coronary heart disease or the corresponding risk, as well as for high-risk patients (e.g., those with a 10-year coronary heart disease risk of more than 20%) with no known coronary heart disease (Mahmood et al., 2009).

For patients who cannot tolerate statins after a heart attack, omega-3 fatty acids may be an alternative option. Niacin and fibrates have not been shown to reduce all-cause mortality in secondary prevention, but they may be beneficial additions when statins alone are insufficient to control lipid levels. Alternatively, fibrates reduce triglyceride and fatty acid levels by activating the peroxisomal β-oxidation pathway.

Several botanical medicinal products have been considered to have the potential to lower cholesterol and lipid levels in the body, improve safety profiles by increasing high-density lipoprotein (HDL) levels, and reducing lipid oxidation, such as berberine, which has shown significant effects on hyperlipidemia indices (Zhang et al., 2013; Thomas et al., 2003; Dou et al., 2008). The majority of the global population, particularly in developing countries, still relies on herbal drugs to meet their healthcare needs (Thomas et al., 2003). Health authorities have increasingly recognized the use of herbal medicines, as they are often the only available option in less urbanized areas and are becoming more popular as an alternative management option in developed regions.[Xiao et al; 2012].

ANTIHYPERLIPIDEMIC EFFECTS OF CURCUMIN

Curcumin, the active ingredient in turmeric spice, is widely used in Asian cuisine as a component of curry powder due to its yellow color. It is believed to possess potent anti-inflammatory and antioxidant properties. Practitioners of traditional medicine consider turmeric powder beneficial for various ailments, including anorexia, hepatic disorders, sinusitis, biliary disorders, cancer, coughs, diabetes, Alzheimer's disease, and rheumatism (Aggarwal et al., 2003). Curcumin has been claimed to reduce hyperlipidemia (Babu et al., 1997). A recent study has revealed the hypolipidemic effect of curcumin by decreasing both free fatty acids and triglycerides in the plasma of hyperlipidemic hamsters (Jang et al., 2008). In another study, nutritional curcumin effectively reduced high hepatic and serum triglyceride concentrations in hyperlipidemic rats. A research investigating the use of capsaicin, an active component in red pepper, as a treatment to lower blood cholesterol in hyperlipidemic rats found it ineffective; however, it was found to be reasonably effective when combined with curcumin (Manjunatha et al., 2006). Feeding mice with curcumin (1% w/w) significantly decreased their hepatic triglyceride levels,

suggesting it may be a beneficial therapeutic strategy for managing fatty liver disease associated with obesity and hyperlipidemia (Asai et al., 1999; Ejaz et al., 2009). When hyperlipidemic rats were placed on a curcumin-supplemented diet, there was a significant reduction in the triglyceride content of very low-density lipoprotein (VLDL) but not chylomicrons (Kempaiah et al., 2004; Asai et al., 2001). This indicates that curcumin promotes hepatic triglyceride clearance without interfering with intestinal triglyceride absorption. Consequently, it is recommended that curcumin consumption may be advantageous as an adjunctive approach in the management and prevention of diet-induced obesity and its associated complications. Another study found that curcumin in a nanoemulsion demonstrated significant cholesterol-lowering activity compared to the drug pravastatin and angiotensin-converting enzyme inhibitors, resulting in vasodilation and reduced angiotensin II production. These effects are attributed to enhanced solubility in the nanoemulsion system (Alsamydai et al., 2018). Curcumin also enhances intestinal maltase, lipase, and sucrase activity, reduces pathological outcomes, and is safe from the damage caused by heart attacks. Curcumin increases Ca^{2+} transfer and its release from the heart muscle's sarcoplasmic reticulum, thereby improving calcium homeostasis in cardiac muscles. Curcumin was found to cause a significant reduction in cholesterol levels in hypercholesterolemic rats. The antioxidant activity of curcumin concentrates vascular dementia in the nervous system, and its therapeutic potential for heart muscle dysfunction is recommended. (Honda *et al.,* 2006)

FREE RADICALS AND ITS EFFECTS IN HUMAN BODY

Oxygen serves as a fundamental requirement for aerobic metabolism and cellular viability across biological systems. During mitochondrial respiration, cells utilize oxygen

for adenosine triphosphate synthesis, generating reactive intermediates known as free radicals as metabolic byproducts. While these species serve beneficial functions at physiological concentrations, excessive accumulation precipitates oxidative stress-mediated tissue damage.

Free radicals are characterized as molecular entities containing unpaired electrons in their outermost orbitals, rendering them highly reactive and capable of initiating cascade reactions (Sen et al., 2010). Their origins encompass both endogenous and exogenous sources. Endogenous generation occurs through intracellular auto-oxidation processes, while exogenous sources include environmental pollutants, organic solvents, pesticides, tobacco combustion products, and anesthetic agents. Cellular sites of free radical production span mitochondria, endoplasmic reticulum, peroxisomes, lysosomes, plasma membranes, and cytosolic compartments (Machlin et al., 1987).

Reactive oxygen species (ROS) represents a collective term encompassing oxidant molecules and free radicals capable of generating additional reactive intermediates. Intracellular ROS production primarily involves superoxide and nitric oxide radicals. Under normal physiological conditions, approximately 2% of consumed oxygen undergoes conversion to superoxide through phagocytic activity and mitochondrial electron transport (Sen et al., 2010).Reactive nitrogen species, particularly nitric oxide, contribute significantly to free radical biology. Nitric oxide functions as a gaseous signaling molecule regulating vascular tone, neurotransmission, smooth muscle relaxation, host defense, and immune modulation. Excessive reactive nitrogen species production results in nitrosative stress (Valko et al., 2007), particularly during inflammatory responses.

Reactive nitrogen species is richly formed throughout inflammatory processes. Reactive oxygen species proportion enhances during exercise, infections, exposure to pollutants, ionizing radiation and ultraviolet light etc. Characteristically, little concentration of reactive oxygen species is necessary for usual physiological purposes like cellular expansion, gene appearance, and protection against infection. Occasionally they too perform as the restorative agents for bio-chemical procedures inside the cell [Machlin et al; 1987] Three primary partially-reduced oxygen intermediates emerge from enzymatic and non-enzymatic electron transfer processes:

Superoxideanion: Generated through continuous oxygen auto-oxidation during mitochondrial electron transport, representing the least reactive yet most abundant free radical species in humans, serving as a precursor for subsequent radical formation.

Hydrogen Peroxide: Metabolized to water through glutathione peroxidase and catalase enzymatic activity.

Hydroxyl Radical: The most reactive free radical species, causing membrane and lipoprotein damage through lipid peroxidation. Low-density lipoprotein oxidation contributes significantly to atherogenesis. Hydroxyl radicals form through water radiolysis and hydrogen peroxide interaction with ferrous ions via the Fenton reaction (Harsh et al., 2010).Uncontrolled ROS production leads to cellular accumulation and oxidative stress. Consequently, cells have evolved sophisticated protective mechanisms against ROS-mediated damage through antioxidant defense systems that regulate ROS generation. Antioxidants are defined as substances present at low concentrations that significantly inhibit or prevent oxidation of susceptible substrates (Scheibmeir et al., 2005).Antioxidant efficacy derives from their ability to donate electrons to ROS, neutralizing their deleterious effects. Cellular antioxidant systems operate at three

distinct levels: (1) prevention through minimizing reactive species formation (e.g., deferoxamine), (2) scavenging through catalytic and non-catalytic mechanisms (e.g., α-tocopherol, ascorbic acid), and (3) repair through restoration of damaged molecular targets (e.g., glutathione) especially curcumin nanocrystals (Xue et al., 2025).

Antioxidant systems comprise two primary categories: enzymatic and non-enzymatic components. Enzymatic antioxidants include glutathione peroxidase, catalase, and superoxide dismutase, serving as primary cellular defenses through catalytic conversion of ROS to less reactive species (Sireesha et al., 2006). Secondary protection involves low molecular weight molecules including α-tocopherol, ascorbate, glutathione, and bilirubin, which either directly scavenge ROS or prevent their formation through sequestration of redox-active transition metals such as copper and iron (Scheibmeir et al., 2005).

ANTIOXIDANT EFFECTS OF CURCUMIN

Curcumin demonstrates potent antioxidant activity through multiple complementary mechanisms. The compound effectively scavenges reactive oxygen species and free radicals that contribute to cellular membrane damage, DNA alterations, and apoptotic cell death. Beyond direct radical neutralization, curcumin modulates inflammatory pathways by inhibiting key pro-inflammatory enzymes and prevents platelet aggregation, thereby reducing thrombotic risk.Recent investigations by Lahan et al. (2024) demonstrated that curcumin-based nanoconjugate formulations effectively suppress reactive oxygen species formation through enhanced antioxidant mechanisms. These engineered protein-curcumin complexes exhibit selective targeting capabilities against pulmonary malignancies, offering potential therapeutic advantages in lung cancer treatment.Oxidative stress represents a fundamental pathogenic mechanism

underlying aging processes and numerous disease states. Free radicals generated through normal cellular metabolism can react with endogenous biomolecules, causing cumulative cellular damage. Curcumin's dual mechanism involves both direct free radical scavenging and enhancement of endogenous antioxidant defense systems, potentially representing one of its most clinically significant therapeutic properties.

Early investigations by Sharma and colleagues (1976) established curcumin's antioxidant capabilities, with subsequent studies demonstrating its efficacy as an oxygen radical scavenger (Ruby et al., 1995; Subramanian et al., 1994) and its protective effects against hemoglobin oxidation (Unnikrishnan et al., 1995). Both lipophilic and hydrophilic turmeric extracts exhibit antioxidant activity comparable to vitamins E and C. Dikshit et al. (1995) demonstrated that curcumin pretreatment attenuated ischemia-induced cardiac alterations in experimental models.

In vitro studies utilizing bovine aortic endothelial cells revealed that Curcuma longa exposure enhanced cellular resistance to oxidative injury through upregulation of heme oxygenase-1, a cytoprotective stress response protein (Mortellini et al., 2000)

CONCLUSION

Curcuma longa represents a rich botanical source of bioactive phytochemicals, with curcumin serving as the primary therapeutic constituent responsible for its diverse pharmacological properties. Despite extensive preclinical and clinical research examining turmeric's medicinal applications, significant knowledge gaps remain regarding optimal therapeutic utilization and clinical translation.

Future research priorities should encompass comprehensive investigation of novel therapeutic indications, development of advanced pharmaceutical formulations, and elucidation of detailed pharmacokinetic profiles. Critical areas requiring systematic

evaluation include mechanism-based drug interactions, food-drug interactions, dose-limiting toxicities, and establishment of evidence-based dosing regimens. Such investigations are essential for developing clinically viable curcumin-based therapeutics that can benefit broader patient populations.

Both rhizome and foliar extracts demonstrate promising therapeutic potential across multiple disease states. However, the primary obstacle limiting curcumin's clinical application remains its inherently poor oral bioavailability, characterized by rapid hepatic metabolism and limited systemic absorption. Addressing this limitation through innovative delivery systems, pharmaceutical co-formulations, or structural modifications represents a critical research imperative for realizing curcumin's full therapeutic potential in clinical practice.

REFERENCES

1- Aggarwal B, Kumar A, Bharti A. Anticancer potential of curcumin: Preclinical and clinical studies. *Anticancer Res*. 2003;23:363–398.
2- Akbik D, Ghadiri M, Chrzanowski W and Rohanizadeh R: Curcumin as a wound healing agent. Life Sciences 2014; 116(1): 1-7.
3- Alsamydai, A.; Jaber, N. Pharmacological aspects of curcumin: Review article. Int. J. Pharmacogn.2018, 5, 313–326.
4- Ammon HP, Wahl MA. Pharmacology of *Curcuma longa*. Planta Med 1991;57:1-7.
5- Ammon HP, Anazodo MI, Safayhi H, Dhawan BN, Srimal RC. Curcumin: A potent inhibitor of leukotriene B4 formation in rat peritoneal polymorphonuclear neutrophils (PMNL). Planta Med 1992;58:226.

6- Asai A, Nakagawa K, Miyazawa T. Antioxidative effects of turmeric, rosemary and capsicum extracts on membrane phospholipid peroxidation and liver lipid metabolism in mice. BiosciBiotechnolBiochem. 1999;63:2118 2122

7- Asai A, Miyazawa T. Dietary curcuminoids prevent high-fat diet-induced lipid accumulation in rat liver and epididymal adipose tissue. J Nutr. 2001;131:2932–2935.

8- Babu P, Srinivasan K. Hypolipidemic action of curcumin, the active principle of turmeric *Curcuma longa* in streptozotocin induced diabetic rats. *Mol. Cell. Biochem*. 1997;166:169–175.

9- Bagchi, A.2012. Extraction of Curcumin. IOSR Journal of Environmental Science Toxicology Food Technology. 1:1–16.

10- Bai, Q., Hu, F., Gou, S., Gao, Q., Wang, S., Zhang, W., ... & Lu, T. (2024). Curcumin-loaded chitosan-based hydrogels accelerating S. aureus-infected wound healing. *International Journal of Biological Macromolecules*, *259*, 129111.

11- Barrie J, Watson T, Stear M, Nash A. Plasma cholesterol and lipoprotein concentrations in the dog: the effects of age, breed, gender and endocrine disease. Journal of small animal practice. 1993; 34: 507-512.

12- Bauer JE. Lipoprotein-Mediated Transport of Dietary and Synthesized Lipids And Lipid Abnormalities of Dogs and Cats. J Am Vet Med Assoc. 2004; 224: 668-675.

13- Chattopadhyay I, Biswas K, Bandyopadhyay U, Banerjee RK. Turmeric and curcumin: Biological actions and medicinal applications. Curr Sci India 2004;87:44-53.

14- Chuengsamarn S, Rattanamongkolgul S, Luechapudiporn R, Phisalaphong C and Jirawatnotai S: Curcumin extract for prevention of type 2 diabetes. Diabetes Care 2012; 35(11): 2121-2127.

15-Dikshit M, Rastogi L, Shukla R, Srimal RC. Prevention of ischaemia induced biochemical changes by curcumin and quinidine in the cat heart. *Indian J Med Res*. 1995;101:31-35

16-Dixon R M, Reid SW, Mooney CT. Epidemiological, clinical, haematological and biochemical characteristics of canine hypothyroidism. Vet Rec. 1999; 145: 481-487.

17-Dou XB, Wo XD, Fan CL. Progress of research in treatment of hyperlipidemia by monomer or compound recipe of chinese herbal medicine. Chin J Integr Med. 2008; 14: 71-75.

18-Ejaz A, Wu D, Kwan P, Meydani M. Curcumin inhibits adipogenesis in 3T3-L1 adipocytes and angiogenesis and obesity in C57/BL mice. J Nutr. 2009;139:919–925.

19-Feldman EC, Nelson RW, Reusch C, Scott-Moncrieff JC. Canine and feline endocrinology. Elsevier health sciences. 2014.

20-Ford RB. Clinical management of lipemic patients. The compendium on continuing education for the practicing veterinarian (USA). 1996.

21-Goel A, Kunnumakkara AB, Aggarwal BB. Curcumin as ''Curcumin'': From kitchen to clinic. *Biochemical Pharmacology*.2008;75(4):787-809.

22-Gómez-Estaca J, Balaguer MP, López-Carballo G, Gavara R and Hernández-Muñoz P: Improving antioxidant and antimicrobial properties of curcumin by means of encapsulation in gelatin through electrohydrodynamic atomization. Food Hydrocolloids 2017; 70: 313-320

23-Govindarajan VS. Turmeric--chemistry, technology, and quality. Crit Rev Food Sci Nutr 1980;12:199-301.

24-Gupta SC, Patchva S and Aggarwal BB: Therapeutic roles of curcumin: lessons learned from clinical trials. The AAPS Journal 2013; 15(1): 195-218.

25-Harsh Mohan, Cell Injury and cellular Adaptations. In: Textbook of Pathology. New Delhi: Jaypee Brothers medical publishers; 2010. p. 21-34.

26-Holder GM, Plummer JL, Ryan AJ. The metabolism and excretion of curcumin (1,7,-bis(4-hydroxy-3-methoxyphenyl)-1,6- hepadiene-3,5-dione) in rat. *Xenobiotica*. 1978;8:761–768.

27-Honda, S., Aoki, F., Tanaka, H., Kishida, H., Nishiyama, T., Okada, S., Matsumoto, I., Abe, K., Mae, T.2006. Effects of ingested turmeric oleoresin on glucose and lipid metabolisms in obese diabetic mice: a DNA microarray study. Journal of Agriculture and Food Chemistry. 54(24):9055-62.

28-Hu S, Maiti P, Ma Q, Zuo X, Jones MR, Cole GM and Frautschy SA: Clinical development of curcumin in neurodegenerative disease. Expert Review of Neuro Therapeutics 2015; 15(6): 629-637

29-Jamil, Q. U. A., Iqbal, S. M., Jaeger, W., &Studenik, C. (2018). Vasodilating, spasmolytic, inotropic and chronotropic activities of curcuminoids from Curcuma longa in isolated organ preparations of guinea pigs. *Journal of Physiology and Pharmacology*, *69*(3).

30-Jang EM, Choi MS, Jung UJ, et al. Beneficial effects of curcumin on hyperlipidemia and insulin resistance in high-fat-fed hamsters. Metabolism. 2008;57:1576–1583.

31-Johnson MC. Hyperlipidemia disorders in dogs. Compendium on continuing education for the practicing veterinarian. 2005; 27: 361-364.

32-Kant V, Gopal A, Pathak NN, Kumar P, Tandan SK and Kumar D: Antioxidant and anti-inflammatory potential of curcumin accelerated the cutaneous wound healing in streptozotocin-induced diabetic rats. International Immuno -pharmacology 2014; 20(2): 322-330.

33-Karam I, Ma N, Liu XW, Li SH, Kong XJ, Li JY, et.al. Regulation Effect of Aspirin Eugenol Ester on Blood Lipids In Wistar Rats With Hyperlipidemia. BMC Vet Res. 2015; 11: 217.

34-Kempaiah RK, Srinivasan K. Influence of dietary curcumin, capsaicin and garlic on the antioxidant status of red blood cells and the liver in high-fat-fed rats. Ann Nutr Metab. 2004;48:314–320.

35-Kharat M, Du Z, Zhang G and McClements DJ: Physical and chemical stability of curcumin in aqueous solutions and emulsions: Impact of pH, temperature and molecular environment. Journal of Agricultural and Food Chemistry 2017; 65(8): 1525-1532.

36-Kumar V, Abbas A K, Fausto N Cellular Adaptations, cell injury and cell death. In: Robbins and Cotran, editors. Pathologic basis of disease. Philadelphia: Saunders; 2009. p. 15-18.

37-Lahan, M., Saikia, T., Dutta, K., Baishya, R., Bharali, A., Baruah, S., ... & Sahu, B. P. (2024). Multifunctional approach with LHRH-mediated PLGA nanoconjugate for site-specific codelivery of curcumin and BCL2 siRNA in mice lung cancer. Future Journal of Pharmaceutical Sciences, 10(1), 163.

38-Machlin L J and Bendich A. Free radical tissue damage: protective role of antioxidant nutrients. Symposium presented by the American Institute of nutrition at the 71st Annual meeting of the Federation of American Societies for Exprimental Biology; 1987 April 2; Washington, DC.

39-Mahmood ZA, Ahmed SW, Sualeh M, Mahmood S. Hyperlipidemia Development and Consequences. Medical Channel. 2009; 5: 14-17.

40-Magi E, Sahk M. 2003. Use of herbal medicine principle in local conditions. Agraarteadus. 14:172–178.

41-Manjunatha H, Srinivasan K. Protective effect of dietary curcumin and capsaicin on induced oxidation of low-density lipoprotein, iron-induced hepatotoxicity and carrageenaninduced inflammation in experimental rats. FEBS J.2006;273:4528–4537.

42-Mith SC, Jackson R, Pearson TA, Fuster V, Yusuf S, Faergeman O, et.al.. Principles for National and Regional Guidelines on Cardiovascular Disease Prevention a Scientific Statement From The World Heart and Stroke Forum. Circulation. 2004; 109: 3112-3121

43-Mortellini R, Foresti R, Bassi R, Green CJ. Curcumin, an antioxidant and anti-inflammatory agent, induces heme oxygenase-1 and protects endothelial cells against oxidative stress. *Free Radic Biol Med*. 2000;28:1303-12.

44-Naito M, Wu X, Normura H, Kodama M, Kato Y, OsaswaT.The protective effect of tetrahydrocurcumin on oxidative stress in cholesterol-fed rabbits. *J. Atheroscler. Thromb*. 2002;9:243–250.

45-Nelson R, Turnwald G, Willard M. Endocrine, Metabolic, and Lipid Disorders. Small Animal Clinical Diagnosis by Laboratory Methods. Saunders St. Louis, Missouri. 2004; 165-207.

46-Noorafshan A and Ashkani-Esfahani S: A review of therapeutic effects of curcumin. Current Pharmaceutical Design 2013; 19(11): 2032-2046.

47-Okada K, Wangpoengtrakul C, Tanaka T, Toyokuni S, Uchida K, Osawa T. Curcumin and especially tetrahydrocurcumin ameliorate oxidative stress-induced renal injury in mice. *J. Nutr*. 2001;31:2090–2095.

48-Panciera DL. Hypothyroidism in dogs: 66 Cases (1987-1992). J Am Vet Med Assoc. 1994; 204: 761-767

49-Pari L, Murugan P. Protective role of tetrahydrocurcumin against erythromycin estolate induced hepatotoxicity. *Pharmacol.* Res. 2004;49:481–486.

50-Parveen, A.L., Syed, W.A., Vivek P., Bashir A. 2017. Role of turmeric in management of alveolar osteitis (dry socket): A randomised clinical study. Journal of Oral Biology and Craniofacial Researchhttp://dx.doi.org/10.1016/j.jobcr.2017.08.005

51-Pawar H, Karde M, Mundle N, Jadhav P and Mehra K: Phytochemical evaluation and curcumin content determination of turmeric rhizomes collected from Bhandara District of Maharashtra (India). Med. Chem 2014; 4(8): 588-591.

52-Peterson ME. Canine and Feline Endocrinology and Reproduction. Journal of Veterinary Internal Medicine. 1988; 2: 162-162

53-Prasad S, Tyagi AK and Aggarwal BB: Recent developments in delivery, bioavailability, absorption and metabolism of curcumin: the golden pigment from golden spice. Cancer research and treatment: Official Journal of Korean Cancer Association 2014; 46(1): 2.

54-Ravindran PN, Nirmal Babu K, Sivaraman K. Turmeric. The golden spice of life. In: Turmeric. The Genus Curcuma. Boca Raton, FL, USA: CRC Press; 2007. p. 1-14.

55-Rheim FA, Ragab AA, Hamdy HED and Hammam FM: Evaluation of DNA damage *in-vivo* by comet assay and chromosomal aberrations for pyrethroid insecticide and the antimutagenic: Role of curcumin. The Egyptian Journal of Hospital Medicine 2015; 59: 172-181.

56-Rogers WA, Donovan EF, Kociba GJ. Lipids and lipoproteins in normal dogs and in dogs with secondary hyperlipoproteinemia. J Am Vet Med Assoc. 1975; 166: 1092-1100.

57-Rogers WA. Lipemia in the dog. Vet Clin North Am. 1977; 7: 637-647.

58-Ruby AJ, Kuttan G, Dinesh Babu K, Rajasekharan KN, Kuttan R. Antitumor and antioxidant activity of natural curcuminoids. Cancer Lett. 1995; 94:79-83

59-Rungseesantivanon S, Thenchaisri N, Ruangvejvorachai P and Patumraj S: Curcumin supplementation could improve diabetes-induced endothelial dysfunction associated with decreased vascular superoxide production and PKC inhibition. BMC Complementary and Alternative Medicine 2010; 10: 57-57.

60-Scheibmeir H D, Christensen K, Whitaker H S, JegaethesanJ,Clancy R, Pierce J D. A review of free radicals and antioxidants for critical care nurses. Intensive and Critical Care Nursing. 2005; 21: 24-28

61-Sen S, Chakraborty R, Sridhar C, Reddy Y S R, De B. Free radicals, antioxidants, Diseases and phytomedicines : Current status and Future prospect. International Journal of Pharmaceutical Sciences Review and Research. 2010; 3(1): 91-100.

62-Sharma OP. Antioxidant activity of curcumin and related compounds. Biochem. Pharmacol. 1976; 25:1811-1812.

63-Sireesha K. Evaluation of Adaptogenic activity of Ocimum Sanctum by invivo and invitro methods. M.Pharm. Thesis, Dept of Pharmacology, Roland Institute of Pharmaceutical Sciences, Berhampur, Orissa. (2006

64-Stone NJ. Lipid management: current diet and drug treatment options. The american journal of medicine. 1996; 101: 40-49.

65-Subramanian M, Sreejayan Rao MNA, Devasagayam TPA, Singh BB. Diminution of singlet oxygen induced DNA damage by curcumin and related antioxidants. Mutat. Res., 1994; 311:249-255.

66-Thomas S. Medications that Lower Cholesterol. Journal of Lipid Research. 2003; 33: 79-82.

67-Unnikrishnan MK, Rao MN. Inhibition of nitric-induced oxidation of hemoglobin by curcuminoids. Pharmazie, 1995; 50:490-492.

68-Valko M, Leibfritz D, Moncol J, Cronin M T D, Mazur M, Telser J. Free radicals and antioxidants in normal physiological functions and human disease. The International Journal of Biochemistry and Cell Biology. 2007(39) 44-84.

69-Wang Q, Tang XN, Wang L, Yenari MA, Ying W, Goh BC, et.al. Effects of high dose of simvastatin on levels of dopamine and its reuptake in prefrontal cortex and striatum among sd rats. Neuroscilett. 2006; 408: 189-193.

70-Watson T, Barrie j. Lipoprotein metabolism and hyperlipidaemia in the clog and cat: a review. Journal of small animal practice. 1993; 34: 479-487.

71-Whitney MS. Evaluation of Hyperlipidemias in Dogs and Cats. Semin Vet Med Surg (Small Anim). 1992; 7: 292-300.

72-Wilson DE, Chan IF, Elstad NL, Peric-Golia L, Hejazi J, Albu DS. et.al. Apolipoprotein e-containing lipoproteins and lipoprotein remnants in experimental canine diabetes. Diabetes. 1986; 35: 933-942.

73-Xenoulis PG, Steiner JM. Lipid Metabolism and Hyperlipidemia In Dogs. The Veterinary Journal. 2010; 183: 12-21

74-Xiao HB, Sun ZL, Zhang HB, Zhang DS. Berberine inhibits dyslipidemia in c57bl/6 mice with lipopolysaccharide induced inflammation. Pharmacol rep. 2012; 64: 889-895.

75-Xu QY, Liu yH, Zhang Q, Ma B, Yang ZD, Liu L, et.al. Metabolomic Analysis of Simvastatin and Fenofibrate Intervention in High-Lipid Diet-Induced Hyperlipidemia Rats. Acta Pharmacol Sin. 2014; 35: 1265-1273.

76-Xue, M., Tian, Y., Zhang, H., Dai, S., Wu, Y., Jin, J., & Chen, J. (2025). Curcumin nanocrystals ameliorate ferroptosis of diabetic nephropathy through glutathione peroxidase 4. *Frontiers in Pharmacology*, *15*, 1508312.

77-Yadav, S. K., Sah, A. K., Jha, R. K., Sah, P., & Shah, D. K. (2013). Turmeric (curcumin) remedies gastroprotective action. *Pharmacognosy reviews*, *7*(13), 42.

78-Zhang X, Wu C, Wu H, Sheng L, Su Y, Zhang X, et.al. Anti-hyperlipidemic effects and potential mechanisms of action of the caffeoylquinic acid-rich pandanus tectorius fruit extract in hamsters fed a high fat-diet. Plos one. 2013; 8: e61922.