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Turmeric: A miraculous Drug

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ABSTRACT

Turmeric is a traditional spice that is made from the rhizomes of the ginger family member Curcuma longa (Zingiberaceae). Turmeric has long been utilised in India for medical purposes and is often referred to as the "Golden Spice of India." Traditional Chinese medicine has prescribed it as a home cure for several illnesses, including rheumatism, sinusitis, anorexia, cough, diabetic wounds, hepatic disorders, and biliary disorders. A wide range of biological effects is demonstrated by turmeric and its compounds, primarily curcumin and essential oils, in addition to its use as a spice and a color. These include its anti-inflammatory, antioxidant, anti-carcinogenic, anti-mutagenic, anti-clotting, antifertility, anti-diabetic, anti-bacterial, anti-fungal, antiprotozoal, antiviral, anti-fibrotic, anti-venom, antiulcer, hypotensive, and hypocholesteremic properties. Researchers' discovery that the herb may have anti-inflammatory and antioxidant qualities sparked modern interest in turmeric in the 1970s. According to safety assessment studies, both turmeric and curcumin are well tolerated at very high doses without producing any adverse consequences. To treat a variety of disorders, contemporary medication may one day be developed using turmeric and its ingredients.

Keywords: *Turmeric, curcumin, antioxidant, anticancer, Ayurveda.*

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INTRODUCTION

Since the beginning of time, people have employed herbal items for a variety of purposes. Natural products have existed for billions of years and have coevolved with earth life. Ten plants out of thousands produce secondary metabolites that protect against different illnesses and infections. Since ancient times, herbal medicines have been important in advancing health. Currently, the Indian system of holistic medicine is known as Ayurveda and uses primarily plant-based medicines or formulations to treat a variety of illnesses, including cancer. Currently, small-molecule medications are being distributed all over the world, and the majority of them have natural product origins [1-3]. The Arabic plant known as Kurkum gave rise to the Latin name of turmeric, Curcuma longa. Sanskrit has many names for turmeric, including "Haridra" (The Yellow One), "Gauri" (The One with a Light and Shining Face), "Kanchani" (The Golden Goddess), and "Aushadhi" (Herb). The most well-known names in India are "Jiang Huang" in Chinese and "Haldi" ("Yellow") in Hindi. The two types of turmeric differ in that some have softer, larger, lighter-colored, and longer rhizomes that are primarily used for eating, while others have hard, rich-colored, oval rhizomes known as "Lokahandi Halad" that are used predominantly for dying.

Since ancient times, turmeric has been designated as a household herb and is utilised in a variety of folklore, traditional, over-the-counter (OTC), and pharmaceutical medications. To regulate health, the rhizome is taken orally. It also works as a treatment for dyspepsia and diarrhea thanks to its choleretic activity, which increased bile flow into the intestine [4-6]. To eliminate bacteria, fungi, and other pathogenic germs, heal wounds, and lessen itching in skin conditions; turmeric is dissolved in water and applied to the skin as a paste. Additionally, it is fried in coconut oil and applied to wounds as an astringent. Additionally, ladies have applied a mixture of turmeric and honey to their body skin as cosmetics. A baby's conjunctivitis can be treated by combining water extract of turmeric powder with breast milk. Rhizomes are grown to cultivate turmeric in agricultural fields. The wet season, particularly the months of May through July, is the best time to cultivate turmeric. Rhizomes persist underground and their leaves become darkened off in the winter. The plant regenerates and grows throughout the following wet season. The crop is harvested 7 to 9 months after it was planted, typically between December and February. Turmeric is recognised as a primary healthcare essential medication by the Ministry of Public Health. One of the five medical plants, turmeric is frequently used as a standalone medication, meaning it is not combined with other plant components. Approximately 39.8 tonnes of turmeric are shipped each year as a spice and condiment. The traditional medical sector employs it (approximately 6.036 tonnes per year). Earth, water, air, and fire were the four elements our ancestors believed made up the human body. Turmeric improves health by controlling the fire elements, which are a sort of digestion. The tropical plant curcuma longa is widely grown in Asia, including India, China, and other nations with suitable conditions [7-9].

Curcuma longa is a perennial herb and a member of the Zingiberaceae family. It has oblong, tufted leaves and can get as tall as one meter. Rhizomes are first boiled, then dried, and finally ground to create the yellow-colored spice. This species of plant is grown on a large scale in Asian countries. An important part of turmeric has been shown to stop carcinogenesis at three different stages: the growth of tumours, the formation of new blood vessels in tumours, and the promotion of new tumours [10]. Turmeric has been used in different parts of the world for hundreds of years. It is made from the dried powder of the rhizome of the Curcuma longa plant. It has many biological effects, such as antioxidant, anti-inflammatory, anti-cancer, anti-growth, anti-arthritic, anti-atherosclerosis, antidepressant, anti-aging, anti-diabetic, antimicrobial, wound healing, and memory-enhancing effects. Curcumin is one of the most important parts of turmeric. It has been studied and used a lot over the past 10 years. Curcumin is an active part of turmeric that gives it its yellow colour. It is found in 2 to 8% of the rhizomes. Curcumin is a curcuminoid that doesn't like water and dissolves well in organic solvents like DMSO, ethanol, methanol, or acetone. Because of this, ethanol extraction is used to get curcumin out of turmeric powder [9, 11, 12]. In Asian cooking, curcuma longa is used to add colour to cheese, butter, yoghurt, and other foods. Curcumin also has a wide range of biological and pharmaceutical effects. Chemically, it is a bis α, β-unsaturated βdiketone and is commonly called as diferuloylmethane . It is a keto-enol tautomer, with the keto form in acidic and neutral solutions and the stable enol form in alkaline solutions. Several studies have shown that curcumin can be used as an anti-inflammatory and antioxidant. Many studies have shown that curcumin also affects the way enzymes in cells work and how new blood vessels form. In 2001, the first study was done on curcumin and how much of it was harmful. According to older reports, no toxic effects of curcumin were seen in people who took up to 8 g of curcumin per day [13-16].

Turmeric and Ayurveda

In India, turmeric has been used for natural treatment for 5,000 years. It has also been utilised for many years in Ayurveda. There are 46 known synonyms for turmeric, including "ptta" (yellow), "gauri" (bright), and all of these words denote "night." This comes from the custom of married ladies applying turmeric to their cheeks in the evening in anticipation of Lakshmi's coming (The Goddess of Prosperity). Turmeric is utilised as a healing drug in Ayurveda and is commonly found as creams, lotions, pastes, and ointments. It can also be taken orally in the form of fresh juice, boiled tea, tinctures, or powder. For example, heated milk with turmeric and sugar for cold remedies and turmeric juice for treating wounds, bruises, and

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leech bites are examples of how ancient Ayurvedic medicine has developed turmeric for use in caring for and improving health. Within a few minutes, the turmeric smoke was utilised to treat scorpion stings [17, 18]. Burned turmeric fumes could be inhaled to instantly relieve congestion and let go of enormous volumes of mucus. In the kitchen, a pinch of turmeric also served as an insect deterrent. Ringworm, itching, eczema, and any other parasite skin issues were treated with a paste made of turmeric, either by alone or in combination with neem (Azadirachta indica) leaves. Turmeric pastes were also applied to cut the placenta after childbirth and were used to treat malaria, smallpox, chickenpox, shingles, ulcers, conjunctivitis, skin blemishes, and ulcerative colitis. Turmeric contains hundreds of molecular components, each of which has a unique biological activity. Antibiotics, 14 cancer preventives, 12 anti-tumor, 12 anti-inflammatories, and at least 20 distinct molecules of antioxidants are among them. About 326 recognised biological actions of turmeric were described by one database. The rhizomes have a minimum content of 70% carbs, 7% protein, 4% minerals, and 4% essential oils. It also includes vitamins, other alkaloids, and roughly 1% resin [2, 19, 20]. Curcumin, which makes up 2 to 5 percent of the active ingredients in turmeric, is found in the rhizomes. Science and Turmeric As scientists become more aware of the value of turmeric in the treatment of numerous contemporary diseases, their interest in the spice grows. Numerous research has been done on the effects of turmeric on the human body, with cancer receiving the most attention. Turmeric is thought to fight cancer in three different ways: 1) it disarms the conditions and agents that can lead to the disease, 2) it directly aids in maintaining cell integrity when threatened by carcinogens, and 3) it frequently eradicates the tumour as it grows. There are numerous justifications for eliminating cancer. Inhibiting the enzyme Topoisomerase, which is crucial for DNA replication in cancer cells, is one of curcumin's key functions. In the cell's nucleus, "topoisomerase" functions by first binding to supercoiled DNA and then catalysing the passage of one DNA helix through another by creating a temporary double-standard break. As a result, the DNA is split, enabling quick cell reproduction. Curcumin inhibits topoisomerase activity, which prevents the issue from multiplying and spreading. Cancers are also treated with allopathic means, however, turmeric has been discovered to be more effective and to have no negative side effects [21-23]. Recent studies appear to support the idea that combining turmeric with a healthy diet will reduce cell growth. Additionally, turmeric has a special ability to cleanse and nourish the skin and blood. Turmeric applied topically eases discomfort and swelling, speeds up the healing of wounds, and treats a variety of skin conditions, from leprosy to acne. By removing toxins and regenerating the liver, turmeric also defends the liver against diseases and toxins. By promoting bile output and flow, turmeric also helps to keep the liver healthy. The liver function is said to be activated by taking 5 g of turmeric with a glass of whey every morning and evening for a month. Turmeric is traditionally given orally in the final two weeks of pregnancy to hasten a simple delivery and to safeguard the health of the mother and unborn child. When used as an analgesic, turmeric helps to ease labor pain [22]. By boosting intestinal flora and promoting healthy digestion, turmeric is also essential for the entire gastro-intestinal system. It has long been used to treat stomach issues like poor digestion, dyspepsia, parasites, and abdominal pains as well as to balance metabolism, break down fats and proteins, enhance absorption, and support the stomach's ability to secrete digestive acids. Additionally, a carminative, turmeric aids in reducing gas and bloating. Plants that affect digestion are regarded as vital herbs in Ayurveda since they maintain both physical and mental health. As a vulnerary, it also supports the nourishment and healing of mucous membranes and safeguards against substances and foods that harm the stomach and intestines. Turmeric has also been used extensively in cases involving the respiratory system. It defends the lungs from poisons and pollution as an antioxidant [24, 25]. Additionally, it aids in the movement of oxygen from the lungs to the blood. Cough and asthma have traditionally been treated with turmeric and ghee. It additionally benefits the heart in a variety of ways including reducing cholesterol and avoiding atherosclerosis (blockage of arteries that can cause a heart attack or stroke). An animal experiment demonstrated that turmeric decreases cholesterol levels and prevents LDL (the "bad cholesterol" that clogs arteries) from being oxidized. Studies on the efficacy of turmeric in preventing neurological conditions including Multiple Sclerosis and Alzheimer's disease are

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also in progress. Elder Indians who routinely consume turmeric are thought to be free from these diseases [26, 27]. However, compared to Americans, the prevalence of Alzheimer's disease among older and adult populations in India is 4.4 times lower. Overall, it is clear that turmeric can endure time. It is one of the most important players in the prevention of major diseases because of its enormous uses in worship that have been known about and adored by people for generations. More studies are being conducted to support scientifically the claims made by the ancient Indians, who have known for generations that turmeric is one of the most potent herbs on earth. Everyone is advised to regularly consume turmeric whether they are afflicted with an acute or chronic illness, or as a preventive measure [28-32].

The main constituent of turmeric curcumin was isolated first in 1815 and obtained in crystalline form in 1870. It was chemically identified as 1, 6-heptadien-3, 5-dione-1, 7-bis (4-hydroxy-3-methoxyphenyl)-(1E, 6E) or diferuloylmethane. The feruloylmethane of curcumin was synthesised and confirmed by Lampe. The melting temperature 183 0C a molecular formula of $C_{21}H_{20}O_6$, and a molecular weight of 368.37 g/mol of curcumin were recorded. Curcumin pH between 2.5- 7.0 appears brilliant yellow and red at pH > 7. The stability of curcumin relies on the pH levels; at acidic pH levels, curcumin shows stability; at basic pH levels, curcumin degrades into ferulic acid and feruloylmethane. Since curcumin slowly degrades between pH 1-6, the stomach is often where it is found. It has a long history of use in China to treat illnesses linked to stomach pain. Curcumin was utilised to alleviate sprains and swelling in traditional Hindu medicine [1, 33-35]. Curcumin has been used as effective anti-inflammatory medications, and recent studies have demonstrated that it also has several other therapeutic effects against a variety of diseases, including those related to cardiovascular health (protection against myocardial infarction), hypoglycemia, and antiarthritis (protection against rheumatoid arthritis). The exceptionally high safety profile for the health of curcumin is its most compelling and ongoing conventional medicinal usage. Curcumin has not yet been linked to many harmful effects in either humans or animals, which suggests that it is safe to use even at very high dosages [2, 35, 36].

MECHANISMS OF ACTION

Antioxidant Effects

Strong antioxidant activity, comparable to that of vitamins C and E, is demonstrated by turmeric's water- and fat-soluble extracts and its curcumin component. According to research on feline heart ischemia, pretreatment with curcumin lessened the effects of the condition on the heart. Bovine aortic endothelial cells were used in an in vitro experiment to evaluate curcumin's impact on endothelial heme oxygenase-1, an inducible stress protein. Curcumin increased cellular resilience to oxidative damage after an 18-hour incubation [37, 38].

Hepatoprotective Effects

Similar to silymarin, turmeric has been found to have hepatoprotective properties. Studies on animals have shown that turmeric protects the liver from several hepatotoxic insults, such as acetaminophen (paracetamol), carbon tetrachloride (CCl4), galactosamine, and Aspergillus aflatoxin. Turmeric's ability to prevent the production of pro-inflammatory cytokines and act as an antioxidant is what primarily cause turmeric to have a hepatoprotective impact. Administration of curcumin significantly reduced liver injury in test animals when compared to controls in rats with CCl4-induced acute and subacute liver injury. When administered to ducklings with Aspergillus parasiticus infections, turmeric extract 90 percent reduced the growth of the fungus that produces aflatoxin. Additionally, biliary hyperplasia, lipid alterations, and necrosis brought on by the synthesis of aflatoxin were reversed by turmeric and curcumin. By boosting biliary excretion of bile salts, cholesterol, and bilirubin as well as by increasing bile solubility, sodium curcuminate, a salt of curcumin, also exhibits choleretic effects. This may help to prevent and treat cholelithiasis [39-42].

Anti-inflammatory Effects

Curcuma longa contains volatile oils and curcumin, both of which have strong anti-inflammatory properties. It was discovered that oral administration of curcumin was half as efficacious as cortisone or phenylbutazone

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in cases of acute inflammation and one-half as effective in cases of chronic inflammation. Oral treatment of Curcuma longa significantly decreased inflammatory swelling in comparison to controls in rats with Freund's adjuvant-induced arthritis. Curcumin prevented the inflammatory neutrophil aggregation seen in monkeys. The anti-inflammatory activities of C. longa may be explained by its capacity to suppress neutrophil function in inflammatory situations as well as the manufacture of inflammatory prostaglandins from arachidonic acid. To reduce inflammation and itchiness brought on by inflammatory skin disorders and allergies, curcumin may also be applied topically; however, caution must be taken to avoid garment stains caused by the yellow pigment [43, 44].

Anticarcinogenic Effects

Curcumin is able to thwart carcinogenesis at three distinct stages, including tumour promotion, angiogenesis, and tumour growth, in both in vivo and in vitro research investigations using human cell lines and studies on rats and mice. Curcumin prevented the formation of tumours and inhibited cell division in two investigations on colon and prostate cancer. Both in vitro and in vivo investigations have shown that curcumin and turmeric can inhibit the activity of several common mutagens and carcinogens in a variety of cell types. Due to their direct antioxidant and free-radical scavenging properties as well as their capacity to subtly raise glutathione levels, turmeric and curcumin have anticarcinogenic properties. This helps the liver eliminate mutagens and carcinogens and prevents the production of nitrosamine [5, 45-47].

Antimicrobial Effects

Numerous bacteria, parasites, and harmful fungi are inhibited in their growth by curcuma longa essential oil and turmeric extract. The caecal parasite Eimera maxima infected chicks were used in a study that showed meals supplemented with 1% turmeric reduced the severity of minor intestinal lesions and increased weight gain. Another animal experiment using infected guinea pigs with dermatophytes, pathogenic moulds, or yeast discovered that turmeric oil administered topically inhibited the dermatophytes and pathogenic fungi but had no effect on the yeast isolates. The guinea pigs with dermatophyte and fungal infections showed improvements in their lesions, and seven days after using turmeric, the lesions had completely vanished. Additionally, moderate efficacy of curcumin against Plasmodium falciparum and Leishmania major organisms has been discovered [48-50].

Cardiovascular Effects

The cardiovascular system is protected by turmeric by lowering triglyceride and cholesterol levels, reducing the vulnerability of low-density lipoprotein (LDL) to lipid peroxidation, and preventing platelet aggregation. Low dosages of turmeric have been found to have these effects. In addition to reducing plasma cholesterol and triglyceride levels, a study on 18 atherosclerotic rabbits showed that low-dose (1.6-3.2 mg/kg body weight daily) turmeric extract reduced LDL's sensitivity to lipid peroxidation. Even while the reductions in cholesterol and triglyceride levels were less pronounced than they were with the lower dose, the greater dose did not reduce the lipid peroxidation of LDL. The effect of turmeric extract on cholesterol levels may be brought on by a reduction in intestinal absorption of cholesterol and an increase in hepatic conversion of cholesterol to bile acids. The potentiation of prostacyclin synthesis and inhibition of thromboxane synthesis are assumed to be the mechanisms by which C. longa components prevent platelet aggregation [51-53].

Gastrointestinal Effects

In digestive system, Curcuma longa constituents have several beneficial actions. Intestinal spasm was prevented by sodium curcuminate, and pancreatic enzyme production was boosted by the turmeric component p-tolymethylcarbinol. Turmeric has also been demonstrated to greatly increase stomach wall mucus in rats exposed to gastrointestinal insults such as alcohol, stress, indomethacin, pyloric ligation, and reserpine. Immunity is improved by curcumin. If certain cells manage to avoid apoptosis, curcumin can aid the body in fighting cancer. After consuming curcumin, scientists observed that CD4+ T-helper and B-type immune cells were more prevalent in the lining of the colon. Curcumin boosts immunity generally in addition to this localised immunological activation. Researchers in India have shown that

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mice fed curcumin had higher antibody levels and stronger immunological responses [54-56].

Interaction of curcumin with various targets

Curcumin is likely a highly pleiotropic chemical that physically interacts with all of its targets. The action of enzymes, growth factor receptors, metals, albumin, and other substances is inhibited by curcumin, which prevents diseases from progressing more quickly. P-glycoprotein, multidrug resistance protein 1 and 2 (MRP1 and MRP2), glutathione, protein kinase C, ATPase, ErbB2, and alpha1-acid glyocoprotein are only a few of the proteins it connects with (AGP). In vitro and in vivo fibril development that binds to tiny β-amyloid species is prevented by curcumin. Curcumin's irreversible binding to CD13/aminopeptidase N (APN) suppresses both tumour angiogenesis and invasion. Curcumin also demonstrated lipoxygenase inhibition and binding to phosphatidylcholine (PC) micelles in another action [57-59].

Curcumin inhibits the activation of transcription factors

Curcumin plays a vital role to inhibit the activation of several transcription factors like nuclear factor-kB (NF-kB), activated protein-1 (AP-1), signal transducer and activator of transcription (STAT) proteins, peroxisomes proliferation-activated receptor-γ (PPAR-γ), and β-catenin, which regulate gene expression contributing in tumorigenesis, inflammation, cell survival, cell proliferation, invasion, and angiogenesis [60-62].

Curcumin down-regulates the multiple kinase activities

Mutations can activate certain tyrosine kinases, which are involved in the development, growth, and spread of human malignancies that are malignant. Numerous studies have suggested that protein kinases involved in growth signaling cascades are novel targets for chemopreventive methods to treat a variety of human malignancies. The epidermal growth factor receptor (EGFR) and HER2/neu are also overexpressed in many human malignancies, which promotes the growth of cancer cells. In vitro cellular tests with curcumin therapy on the aforementioned conditions revealed suppression of EGFR kinase activity and EGF-induced tyrosine phosphorylation of EGFR in A431 cells and decreased Her2/neuprotein in cells. Curcumin can also break down intracellular HER2 and eliminate its tyrosine kinase activity instead of geldanamycine. Curcumin also inhibits the phosphatidylinositol 3 kinase/AKT pathway, arrests the G2/M cell cycle, and causes non-apoptotic autophagic cell death in malignant glioma cells by altering the Akt and Erk signalling pathways, which causes apoptosis in acute T cell leukemias [63-66].

Curcumin inhibits the expression of growth and metastases promoting genes

Oncogene overexpression promotes the development of tumour cells and serves as a target for chemopreventive regimens. Cyclooxygenase-2 is linked to several malignancies, including breast, lung, and colon cancers (COX-2). The discovery of COX-2 inhibitors has been the focus of research in recent years and it was found that curcumin suppresses COX-2 expression by downregulating NF-kβ, which is required for COX-2 activation [66].

Curcumin inhibits the expression of multiple genes/pathways involved in apoptosis, cell invasion, and adhesion

Additional molecular targets that influence cell adhesion, apoptosis, and invasion are under the control of curcumin. The expression of intracellular cell adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and E-selectin by TNF-α in human umbilical vein endothelial cells is stimulated by curcumin, and curcumin is a highly strong inhibitor of this. Curcumin may be negatively affecting the TNF-α induced signaling event at an early stage by appearing to hinder the induction of steady-state transcription levels of ICAM-1, VCAM-1, and E-selectin. Additionally, studies on human prostate cancer (PC3) and colon cancer (HT-29) cell lines have shown that curcumin has anticancer, chemosensitive, and radiosensitive properties. These properties are mediated by activation of p53 and simultaneous downregulation of MDM2 oncogene expression via the PI3K/mTOR/ETS2 pathway, and by inducing apoptosis, nuclear translocation, and activation of p53 in human neuroblastoma cells [67-69].

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Curcumin regulates the activities of several enzymes mediated tumor growth

In addition to directly controlling gene expression, curcumin also disrupts the actions of enzymes involved in cell proliferation and tumorigenesis. Hemoxygenase-1 (HO-1) gene expression is increased by curcumin, which inhibits fibrosis in anti-Thy1 glomerulonephritis and may have antifibrotic effects on the glomerulus. Similarly, curcumin can also increase HO-1 expression by activating p38, producing reactive oxygen species, and inhibiting phosphatase. Through its impact on Ras protein pathways, curcumin can also inhibit the proliferation of cancerous tumour cells. Ras proteins are isoprenylated at a conserved cysteine residue close to the carboxyl terminus to increase their biological activity (Cys186 in mammalian Ras p21 proteins) [70, 71]. According to earlier research, farnesyl pyrophosphate is likely the source of this isoprenyl group, and Ras oncogene expression may be prevented from changing cells by blocking the mevalonate pathway. Curcumin and its derivatives appear to have a significant part in the system that prevents cells from growing. Another study found that curcumin significantly reduced the activity of xanthine oxidase (XO) in vitro in NIH3T3 cells that had been treated with PMA. With curcumin's strong capacity to suppress PMA increases, one of the main causes of PMA-mediated tumour promotion is thought to be the induction of XO activity, which manifests as the XO protein being directly inactivated [72, 73].

CONCLUSION

Curcumin is widely recognised for its comprehensive health advantages, which mostly seem to be brought about by its anti-inflammatory and antioxidant properties. Curcumin works best when paired with substances like carbs and piperine, which greatly boost its bioavailability. Curcumin may aid in the treatment of oxidative and inflammatory diseases, metabolic syndrome, anti-inflammatory, anxiety, and anti-diabetic disorders, according to research. As a result, recuperation time and subsequent performance in physically active people are facilitated. It may also assist in the management of several pharmacological activities utilised in health and also improve the health for the body benefits human health. Additionally, even those without known medical concerns may benefit from a relatively sufficient dose in terms of their health.

Consent and Ethical Approval

As per university standard guideline, participant consent and ethical approval have been collected and preserved by the authors

Competing interests

Authors have declared that no competing interests exist.

Authors' Contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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