Turmeric

Curcuma longa

Family: Zingiberaceae.

Parts Used: Dried rhizome.

Description: Curcuma domestica Valeton is generally accepted to be the same species as Curcuma longa.[1] A stemless, leafy perennial herb closely resembling ginger (Zingiber officinale) and growing up to 1.5 metres tall. The large, broad, hairless, light green leaves arise from near ground level and are borne at the top of the non-woody underground stem, with overlapping petioles. They are 30- 40 cm long and 8-12 cm wide, and are thin, oval-shaped and elongated. Attractive pale yellow and white bell- shaped flowers emerge in short oblong spikes developing in the centre of the leaves. The fleshy, smooth, branched rhizomes are bright orange outside and bright orange to yellow within. Turmeric is a sterile plant and does not produce any seeds. It is extensively cultivated in India, China, Indonesia, islands of the Caribbean, South America and other tropical countries.[2,3]

Traditional and Empirical Use: Although in medicinal use in Asia for more than 2500 years, turmeric is probably better known in the West as a common yellow spice. It is used as one of the principle, pungent flavouring ingredients in curries and widely used in the food industry as a colouring agent (as a food additive, curcumin's code number on food labels is 100).[4]

Unlike its close botanical relative, ginger, it never caught on in the West as a medicinal herb. Until recently Western medicine viewed turmeric primarily as a spice with minor aromatic digestive stimulant and hepatic stimulant properties indicated, but little used, for functional hepatobiliary disorders. In the 1930s it was mentioned in the classic book A Modern Herbal, the first comprehensive encyclopaedia of herbs to appear since the days of Culpeper (1600s). The author Maude Grieve's only medicinal reference to turmeric is 'it was once a cure for jaundice'. In 1985 the German Commission E approved turmeric root for dyspeptic conditions, although the herb was absent from both the 1983 and 1996 edition of the British Herbal Pharmacopoeia. The long established image of turmeric as a commercial dyestuff, and a component of curry, have been partly responsible for overshadowing its importance as a medicinal herb in the West.[6,7]

The name turmeric originated from the Medieval Latin name terramerita, which became terre merite in French, meaning deserved earth or meritorious earth, a name by which powdered turmeric was known in commerce. Marco Polo, in 1280 A.D., mentioned turmeric as growing in the Fokien region of China and is reported to have said "I have found a plant that has all the qualities of saffron, but it is a root." [8]

Turmeric is known as Haridra (the yellow one) in Sanskrit and holds a place of honour in India's traditional Ayurvedic system of medicine. It has been a mainstay in curries on the Indian subcontinent for thousands of years and gives curry blends their yellow colour. In addition to its role in cooking, the herb was used for the preservation of food and valued more than gold or precious stones. It was later used commercially as a colouring agent for various items including cotton, silk, paper, wood, foods and cosmetics. Touted by researchers as 'Indian solid gold', 'a spice for life' and 'an age old herb for old age', it is considered a symbol of prosperity and known as a cleanser for the whole body. As a sacred and auspicious item, turmeric has become associated with many Hindu customs and traditions and has been used extensively in various Indian ceremonies for millennia. It is used in every part of India during weddings and other religious ceremonies.[9,10,11]

It was highly esteemed by the ancient Indo-European people for its golden-yellow dye resembling sunlight. This culture, known as Arya, worshipped the solar system and attributed special protective properties to those plants, which, like turmeric, contained sun-coloured yellow dyes. In India it can be identified by scores of synonyms, many of which make reference to night. This may be derived from a tradition which required that married women apply turmeric on their cheeks in the evening, in anticipation of a visit by the goddess, Lakshmi, at that time. This custom, still practiced mostly in South India, is probably a remnant of an ancient sun-worship tradition.[12]

Turmeric exemplifies a herb for which clinical applications have evolved over time. Since the time of Ayurveda (1900 BC) numerous therapeutic activities have been assigned to turmeric for a wide variety of diseases and conditions, especially anti-inflammatory, including such ailments as gynaecological problems, gastric problems, hepatic disorders, infectious diseases and blood disorders. Modern science has provided the scientific basis for the use of turmeric against such disorders. Boiled with milk and sugar, it has been a traditional remedy for colds. The inhalation of the fumes of burning turmeric causes copious mucous discharge and is said to give instant relief in chronic catarrh. Externally it has been used in the prevention and treatment of skin diseases. The juice of the fresh rhizome is used in parasitic skin infections and turmeric powder rubbed down with oil has been applied to soften rough skin. In chickenpox a coat of turmeric is applied to facilitate the process of scabbing.[13,14]

Traditional Chinese physicians see turmeric (known as Jiang huang) as a warm, pungent, bitter herb related to the spleen, stomach and liver. Its actions are to regulate and move blood, move, regulate and descend Qi, dispel damp-wind, break up blood stasis and relieve pain. In Chinese medicine it is used for menstrual problems such as amenorrhoea and dysmenorrhoea, pain in the chest, abdomen, muscle and joint complaints, and to support liver function and treat jaundice.[15]

In these two systems of medicine (Ayurveda and Chinese), turmeric has been shown to improve gynaecological conditions such as regulating the female reproductive system, purifying the uterus and breast milk. It has also been shown to help relieve the pain of labour. In the last two weeks of pregnancy the mother should take two to three grams a day in warm organic milk. This old remedy is said to simplify the birth, increase the health of mother and child, and decrease the pain of the birth.16 However, scientific evidence proving these benefits is lacking.[17]

Curcumin, which gives the yellow colour to turmeric, was first isolated by Vogel in 1842, and its chemical structure as diferuloylmethane was determined by Lampe and Milobedeska in 1910. In the 1870s chemists noticed that turmeric's orange-yellow root powder turned reddish brown when exposed to alkaline chemicals. This discovery led to the development of 'turmeric paper', thin strips of tissue brushed with a decoction of turmeric, then dried. During the late 19th century, turmeric paper was used in laboratories around the world to test for alkalinity. Eventually it was replaced by litmus paper which is still used today.[18]

Pharmacological investigations into the anticancer and anti-inflammatory properties of turmeric and its constituents began to attract research interest in the 1980s. Currently, curcumin is regarded as a natural compound of great interest and of considerable therapeutic potential because of its multiple properties which include antioxidant, anti-inflammatory, chemopreventative, antimutagenic, anticarcinogenic, antimetastatic, antiangiogenic and cardioprotective activities. Although initially it was believed that the activities of turmeric were mainly due to curcumin, research conducted during the 2000s and beyond has identified numerous chemical entities from turmeric and modern

science has provided a logical basis for the safety and efficacy of turmeric against human disease.[19,20]

Although this research currently constitutes a rapidly expanding body of literature, a 2003 therapeutic monograph on turmeric by the European Scientific Cooperative on Phytotherapy (ESCOP) echoes the original 1985 Commission E indications for 'symptomatic treatment of mild digestive disturbances and minor biliary dysfunction.[21]

Constituents: To date, around 235 compounds, primarily phenolic compounds and terpenoids, have been identified in turmeric. The following are the most well known. Curcumonoids: Yellow to orange pigments (3-5%), mainly diarylheptanoids, with curcumin (diferuloylmethane or curcumin I), demethoxycurcumin (curcumin II) and bisdemethoxycurcumin (curcumin III) as the main constituents; volatile oil (3-5%) is rich in bisabolane, guaiane and several germacrane-type sesquiterpenes including alpha and beta turmerone, curlone, cucumol and zingiberene; polysaccharide (arabino-galactan ukonan A); calebin A, vanillic acid and vanillin are other phenylpropene and phenolic compounds identified from turmeric. The contents of curcuminoids in turmeric rhizomes vary often with varieties, locations, sources and cultivation conditions, and significant variations have been observed in composition of essential oils of turmeric rhizomes with varieties and geographical locations. Furthermore, both curcuminoids and essential oils vary in content with different extraction methods and under some conditions are unstable with extraction and storage processes. For example curcumin I is absorbed poorly by the gastrointestinal tract and/or undergoes presystematic transformation. As a natural colouring agent, it is known to be unstable particularly under alkaline conditions, light and high temperature. All curcumonoids are stable when they are kept under minimum light conditions. It has been found that the stability of curcumin I in aqueous solution is strongly increased by the presence of some antioxidants. But the presence of other curcuminoids (II and III), which are antioxidants, seem not to prevent degradation of curcumin I. Isolation of pure curcumin I from turmeric is difficult and time-consuming, and thus the commercial "pure" curcumin I is in fact a mixture of at least three curcuminoids. Such curcuminoids can decompose rapidly but curcuminoids in both turmeric powder and extracts are more stable. Ethanol extraction has shown advantages in both effective extraction and stability of active curcuminoids. Among different extraction solvents, ethanol extraction gives the highest yield of curcuminoids. As a result, commercial turmeric products (whole rhizomes, ground turmeric, turmeric oils, turmeric oleoresin and "curcumin") have significant variations in composition of bioactive compounds.[22,23,24,25]

Actions: Anti-inflammatory, anticarcinogenic, antimutagenic, immunomodulator, radioprotective, hepatoprotective, anti-ulcer, hypolipideamic, antiatherogenic, analgesic, antimicrobial, antiviral, antifungal, nephroprotective, antidepressant, antiaging, larvicidal, insecticidal.

Pharmacological Activity: Although much has been published about curcumin, comparatively little is known about turmeric itself. A search of curcumin on Pubmed[26] (a public domain, bibliographic reference source) returns more than 5800 articles, while turmeric returns less than half that, with just over 2500 articles, which on closer inspection are mostly on curcumin. Therefore, data from studies investigating use of turmeric extracts, or other preparations of the whole spice, are limited, especially those comparing the potential of turmeric with curcumin.[27]

Nevertheless, epidemiologic data indicates that some extremely common cancers in the Western world are much less prevalent in regions (e.g. Southeast Asia) where turmeric is widely consumed in the diet.[28]

Cell- based studies have demonstrated the potential of whole turmeric as an antimicrobial, insecticidal, larvicidal, antimutagenic, radioprotector and anticancer agent. Numerous animal studies have shown the potential of this spice against proinflammatory diseases, cancer, neurodegenerative diseases, depression, diabetes, obesity and atherosclerosis. At the molecular level, like curcumin, it has been shown to modulate numerous cell signalling pathways and in more than a dozen human clinical trials turmeric has shown safety and efficacy against numerous human ailments including lupus nephritis, cancer, diabetes, irritable bowel syndrome, acne and fibrosis.[29]

There are numerous ongoing trials evaluating the efficacy of turmeric in humans and there are a number of completed studies, however the results are yet to be published. For example an Iranian study was conducted to see whether turmeric can be effective in the treatment of pruritus in haemodialysis patients with end stage renal failure. Another study investigated whether turmeric is effective in improving diabetic nephropathy and in decreasing the amount of proteinuria and cytokine levels. A phase II clinical trial from France aimed to determine the efficacy and tolerance on 15 days of a turmeric extract (Arantal) in patients with osteoarthritis of the knee (gonarthrosis).[30]

Although turmeric has shown therapeutic efficacy against many human ailments, one of the key problems with turmeric is the poor bioavailability of its constituents. Major reasons contributing to the low plasma and tissue levels of the key constituent of turmeric, curcumin, appear to be due to poor absorption, rapid metabolism and rapid systemic elimination. Many of the animal studies involve parenteral (bypassing the mouth, usually injection) administration and oral curcumin, or turmeric, is likely to be far less active because curcumin is poorly absorbed by the gastrointestinal tract and only trace amounts appear in the blood after oral intake. To improve the bioavailability of curcumin, numerous approaches have been undertaken like the use of piperine that interferes with glucuronidation, the use of liposomal curcumin, curcumin nanoparticles, curcumin phospholipid complex and structural analogues of curcumin. Curcumin may, however, have a local action on the gastrointestinal tract and systemic effects may occur at very low concentrations of curcumin.[31]

Because of the extremely low bioavailability of curcumin the interpretation of some studies is particularly controversial, and the clinical relevance of the numerous pharmacological studies on curcumin (or its intravenous use) is uncertain and remains to be established. The majority of recent scientific studies on turmeric employ purified laboratory- grade diferuloylmethane or curcumin I, which should be noted before extrapolating to mixtures of curcuminoids or to crude whole herb extracts. The biotransformation products of curcumin need to be further studied, since oral doses of curcumin have exerted significant activity in several experimental models and clinical trials.[32,33]

It is for these reasons that this monograph will focus on whole herb studies as opposed to the overwhelming amount of curcumin studies. In relation to this a groundbreaking July 2013 review has identified numerous chemical entities from turmeric other than curcumin. The review states that it is unclear whether all of the activities ascribed to turmeric are due to curcumin or whether other compounds in turmeric can manifest these activities uniquely, additively or synergistically with curcumin. Studies have indicated that turmeric oil, present in turmeric, can enhance the bioavailability of curcumin. Over the past decade studies have indicated that curcumin-free turmeric (CFT) components possess numerous biological activities including anti-inflammatory, anticancer and antidiabetic activities. Elemene derived from turmeric is approved in China for the treatment of cancer. The review focuses on the anticancer and anti-inflammatory activities exhibited by CFT and by some individual components of turmeric, including turmerin, turmerone, elemene, furanodiene, curdione, bisacurone, cyclocurcumin, calebin A and germacrone.[34]

This is a lesson to herbalists not to be reductionist when it comes to their herbs. Traditional herbal medicine is based on the premise that the medicinal activity of herbal products is not due to a single chemical but the combined effect of all its constituents. Even in today's highly sophisticated and technically advanced scientific world, many of these constituents or chemical compounds are still unidentified. However, when extracted in a balanced way, the synergistic activity of all the constituents allows the key compounds to work effectively. The biochemical equilibrium within the herb must be maintained as this has proven effective throughout the ages to both heal bodies and sustain good health. The active ingredient can lose its impact, or become less safe, if used in isolation from the rest of the plant. The effect of the whole plant is greater than its parts.[35]

To summarise curcumin, to date more than 65 human clinical trials of curcumin, which included more than 1000 patients, have been completed, and as many as 35 clinical trials are underway.[36]

Extensive research over the past half century has shown that at a molecular level curcumin (diferuloylmethane) can modulate multiple cell signalling pathways including cell cycle (cyclin D1 and cyclin E), apoptosis (activation of caspases and down-regulation of antiapoptotic gene products), proliferation (HER-2, EGFR, and AP-1), survival (PI3K/AKT pathway), invasion (MMP-9 and adhesion molecules), angiogenesis (VEGF), metastasis (CXCR-4) and inflammation (NF-kappaB, TNF, IL-6, IL-1, COX-2, and 5-LOX). These clinical trials have addressed the pharmacokinetics, safety and efficacy of this nutraceutical against numerous diseases in humans. Some promising effects have been observed in patients with various pro-inflammatory diseases including cancer, cardiovascular disease, arthritis, Alzheimer's disease, psoriasis, uveitis (inflammation of the uvea in the eye), ulcerative proctitis, Crohn's disease, ulcerative colitis, irritable bowel disease, tropical pancreatitis, peptic ulcer, gastric ulcer, idiopathic orbital inflammatory pseudotumour, oral lichen planus, gastric inflammation, vitiligo, psoriasis, acute coronary syndrome, atherosclerosis, diabetes, diabetic nephropathy, diabetic microangiopathy, lupus nephritis, renal conditions, acquired immunodeficiency syndrome, beta-thalassemia, biliary dyskinesia, Dejerine-Sottas disease, cholecystitis and chronic bacterial prostatitis. Curcumin has also shown protection against hepatic conditions, chronic arsenic exposure and alcohol intoxication. In clinical trials, curcumin has been used either alone or in combination with other agents. Various formulations of curcumin, including nanoparticles, liposomal encapsulation, emulsions, capsules, tablets and powder have been examined. Interestingly, 6-gingerol, a natural analogue of curcumin derived from the root of ginger (Zingiber officinalis), exhibits a biologic activity profile similar to that of curcumin.[37,38]

Anti-inflammatory actions: Inflammation, in particular chronic inflammation, has been associated with numerous human chronic diseases including cardiovascular, pulmonary, autoimmune and degenerative diseases cancer and diabetes.[39]

Turmeric is widely used for the treatment of disorders associated with inflammation. A 2013 randomised, single blind, placebo-controlled trial has demonstrated the safety and efficacy of turmeric as a useful treatment option for patients with primary painful knee osteoarthritis (OA). The study showed a significant decrease in use of rescue medication (Paracetamol), which demonstrated turmeric's analgesic potential, along with clinical and subjective improvement, compared to placebo, over a period of 42 days. It was published in Inflammopharmacology, an international journal that concentrates on the mechanisms of action and the use of anti-inflammatory agents. The anti-inflammatory activity of curcuminoids from turmeric is well known however its polysaccharide fraction has not been evaluated until recently. Natural Remedies

Private Limited, a supplier of standardised botanical extracts, recently developed a polysaccharide rich, water soluable extract named Turmacin (NR-INF-02), a novel extract of turmeric devoid of curcuminoids. In order to evaluate the safety and efficacy ofthisextractresearchersfromSt. John'sMedicalCollege, Bangalore conducted the trial. A total of 120 patients (37 males and 83 females) with primary knee OA received either placebo (400 mg twice daily) or Turmacin (500 mg twice daily) or glucosamine sulphate (GS) (750 mg twice daily) alone or combination of Turmacin and GS for 42 days. The efficacy was assessed during the treatment period, on day 21 and day 42. The decrease in severity of pain symptom, and function of affected knee, as primary efficacy outcome measure was assessed using internationally validated methodsincludingVisualAnalog Scale(VAS)andWestern Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale, respectively. The clinical examination of affected joint was measured by an orthopaedic specialist and using a Clinician Global Impression Change (CGIC) scale. The analysis of post-treatment scores following administration of Turmacin using VAS, WOMAC, and CGIC at each clinical visit showed a significant decrease ($p<0.05$ meaning the probability of that happening was less than 1 in 50) compared to placebo. The tolerability and acceptability profile of Turmacin was better during the trial period. This study effectively demonstrated the efficacy of Turmacin for overall joint health as assessed by joint crepitation or popping (37%), joint tenderness (86.2%), joint effusion (100%) and joint movement (83.3%).[40]

Another 2013 study to assess the effects of a herbal supplement on systemic inflammation and antioxidant status in non-dialysis chronic kidney disease (CKD) patients has shown that turmeric and Boswellia serrata are safe and tolerable, and helped to improve the levels of an inflammatory cytokine. CKD is characterised by a continuous reduction in kidney function, increased inflammation, and reduced antioxidant capacity. Sixteen patients with CKD were randomly chosen to receive a herbal supplement composed of turmeric and Boswellia serrata, or placebo. Plasma levels of interleukin-6 (IL-6), tumour necrosis factor-α (TNF-α), glutathione peroxidase (GPx), and serum C-reactive protein (CRP) were measured at baseline and eight weeks. Baseline data demonstrated elevated inflammation and low antioxidant levels. A statistically significant anti-inflammatory effect was observed for IL-6. No significant differences were observed for any other variables.[41]

Lupus nephritis is an inflammation of the kidney caused by systemic lupus erythematosus, a disease of the immune system. The disease is responsive to immunosuppressive and steroid therapy but sometimes the disease relapses. A randomised and placebo-controlled study investigated the effects of oral turmeric supplementation on 24 patients with relapsing or refractory biopsy proven lupus nephritis. With each meal, each patient in the trial group received one capsule for three months, which contained 500 mg turmeric, of which 22.1 mg was the active ingredient curcumin (3 capsules daily). The control group received 3 capsules (1 with each meal) for the same period, which contained starch and were identical in colour and size to capsules given to patients in the trial group. A significant decrease in proteinuria was found in the trial group compared with the control group. Also, systolic blood pressure and haematuria were significantly lower in the trial group after supplementation. The authors concluded that short-term turmeric supplementation can decrease proteinuria, haematuria and systolic blood pressure in patients suffering from relapsing or refractory lupus nephritis and can be used as an adjuvant safe therapy for such patients.[42]

A recent study in India compared the effects of experimental local-drug delivery system containing 2% whole turmeric (gel form) as an adjunct to scaling and root planning (SRP) with the effects observed using SRP alone. SRP is also known as

conventional periodontal therapy, non-surgical periodontal therapy, or deep cleaning, and is the process of removing and/or eliminating the etiologic agents – dental plaque, its products, and calculus – which cause inflammation, thus helping to establish a periodontium that is free of disease. Thirty subjects with chronic localised or generalised periodontitis with pocket depth of 5 to 7 mm were selected for the study. Control sites received SRP alone, while experimental sites received SRP plus 2% whole turmeric gel for seven days. Both groups demonstrated statistically significant reduction in the biomarkers of periodontitis. However a greater reduction was seen in all the parameters in the experimental group in comparison to the control group. The authors of the study concluded that whole turmeric gel can be effectively usedasanadjuncttoSRPandthatwholeturmericismore effective than SRP alone in the treatment of periodontitis.[43]

Research over the past several years using animal models has indicated that turmeric can act as an anti-inflammatory agent by modulating the expression of inflammatory molecules.[44]

The immune-stimulatory and anti- inflammatory activities of a turmeric extract (Turmacin) and its polysaccharide fraction were studied in 2013. Its effects on proliferation, nitric oxide (NO), monocyte chemotactic protein-1 (MCP-1), interleukins (ILs) and prostaglandin (PGE2) levels of mouse splenocytes and mouse macrophage (RAW264.7) cells were determined. The extract increased splenocytes number in presence and absence of lipopolysaccharide (LPS) or concanavalin A. Treatment with the extract showed a significant increase of NO, IL-2, IL-6, IL-10, IL- 12, interferon (IFN) gamma, tumour necrosis factor (TNF) alpha and MCP-1 production in unstimulated mouse splenocytes and mouse macrophages. Interestingly, the extract showed potent inhibitory effect towards release of PGE2 and IL-12 levels in LPS stimulated mouse splenocytes. Further, the extract was fractionated into polysaccharide fraction (F1) and mother liquor (F2) to study their immune-modulatory effects. F1 was found to be more potent than F2 toward inhibiting PGE2 and IL- 12 in LPS stimulated splenocytes. The findings revealed the novel anti-inflammatory property of the extract and its polysaccharide fraction by inhibiting the secretion of IL-12 and PGE2 in vitro.[45]

The administration of turmeric extract arrested the degenerative changes in the bone and joints of collagen-induced arthritic rats.[46] A study to determine the antiarthritic efficacy and mechanism of action of a well-characterised turmeric extract using a rat model of rheumatoid arthritis has demonstrated in vivo efficacy and identified a mechanism of action for the extract that supports further clinical evaluation of turmeric dietary supplements in the treatment of rheumatoid arthritis. The extract profoundly inhibited joint inflammation and periarticular joint destruction in a dose-dependent manner. It also prevented local activation of NF-kappaB and the subsequent expression of NF-kappaB-regulated genes mediating joint inflammation and destruction, including chemokines, cyclooxygenase 2 and receptor activator of nuclear factor kappa B ligand (RANKL). Consistent with these findings, inflammatory cell influx, joint levels of prostaglandin E(2) and periarticular osteoclast formation were inhibited by turmeric extract treatment.[47]

Turmeric was shown to possess anti-inflammatory properties during both N-nitrosodimethylamine administration and Opisthorchis viverrini infection in hamsters. Turmeric exhibited its activity by reducing the aggregation of inflammatory cells surrounding the hepatic bile ducts, which correlates with a decreased serum alanine transaminase level. The decrease in direct bilirubin levels in the hamsters treated with turmeric suggests that turmeric may enhance biliary contraction. The study found that turmeric clearly reduces the inflammatory cells in hamster opisthorchiasis (parasitic disease) at an early stage. This finding may be connected with a reduction in the risk factors of cholangiocarcinoma development.[48]

Turmeric plays a protective role in the development of acute pancreatitis and pancreatitis-associated lung injury a recent study has shown. The effects of turmeric on cerulein-induced acute pancreatitis in mice were studied. The oral administration of turmeric significantly ameliorated the severity of pancreatitis and pancreatitis- associated lung injury, as was shown by the reduction in pancreatic oedema, neutrophil infiltration, vacuolization, necrosis, serum amylase, lipase and cytokine levels and mRNA expression of multiple inflammatory mediators such as interleukin (IL)-1ß and -6 and tumour necrosis factor (TNF)-α. In order to identify the regulatory mechanism of turmeric on cerulein-induced pancreatitis, the authors examined the level of haeme oxygenase HO-1 in the pancreas. They found that the administration of turmeric induced HO-1.[49]

A study of the effect of turmeric extracts on inflammatory mediator production has shown that organic extracts of turmeric exhibited cytotoxicity and inhibited production of lipopolysaccharide induced tumour necrosis factor alpha and prostaglandin E2 in human leukaemia cells.[50] Psoriasis is a chronic inflammatory skin disorder characterised by rapid proliferation of keratinocytes and incomplete keratinisation. Discovery of safer and more effective anti-psoriatic drugs remains an area of active research. An ethanolic extract of turmeric has been shown to possess antipsoriatic activity in a keratinocyte cell line in an in vitro model. Turmeric significantly decreased the expression of colony stimulating factor (CSF)-1, interleukin (IL)-8, NF-kB2, NF-kB1.The study suggested that turmeric might exert its activity by controlling the expression of NF- κB signalling biomarkers.[51]

Antioxidant activity: There are a number of in vitro studies demonstrating turmeric acting as a free radical scavenger. A 2006 study found that in addition to curcumin, turmeric contains the antioxidants protocatechic acid and ferulic acid. Further, turmeric also exhibited significant protection to DNA against oxidative damage as evidenced by migration of DNA on the agarose gel (A principal component of agar, agarose is frequently used in molecular biology for the separation of large molecules, especially DNA).[52]

An aqueous extract of turmeric has been shown to have significant antioxidant activity. Liposomal lipid peroxidation and peroxide induced DNA damage were investigated. Inhibition of lipid peroxidation was studied using 400 microM uric acid, beta-carotene, alpha-tocopherol, curcumin and butylated hydroxyanisole (BHA). Curcumin was as effective an antioxidant as BHA. An aqueous extract of turmeric was also found to be an effective inhibitor. The inhibition obtained using this aqueous extract, incorporated into the liposome itself, was 70% at 300 ng/ microlitre. This indicates the presence of yet another antioxidant in turmeric besides the lipophilic curcumin. The aqueous antioxidant extended 80% protection to DNA against peroxidative injury at 100 ng/ microlitre. This component of turmeric is being characterised and investigated as an antioxidant/ anticlastogen and as an antipromoter.[53]

Another in vitro study provides evidence that turmeric gives protection against oxidative stress induced by hydrogen peroxide in a renal cell line.[54] Another in vitro assay of all fractions of a turmeric extract preparation exhibited pronounced antioxidant activity, which was assigned to the presence of curcumin and other polyphenols.[55] Consumption of an aqueous turmeric extract exhibited hypolipidaemic and antioxidant activities in a hypercholesterolaemic zebrafish model and potently suppressed the incidence of atherosclerosis via its strong antioxidant potential.[56]

One of the most important effects of thyroid hormones (T3 and T4) is the elevation of mitochondrial respiration, producing a hyper-metabolic state with excess

generation of free radicals. It has been shown that tissues in hyperthyroid rats exhibit low antioxidant capacity and high susceptibility to oxidative challenge. Oxidative stress from superoxide ($O_2^{\cdot -}$) and other reactive oxygen species (ROS) contributes to the development of renal insufficiency and in the pathogenesis of renal diseases, producing vascular, glomerular, tubular and interstitial injury. Thyroxine has been reported to induce renal hypertrophy with a rise in the DNA content. However, there is a paucity of information on T3-induced oxidative damage to mammalian kidney in general and with respect to antioxidant treatment in particular. With this background an investigation was designed to compare the effectiveness of turmeric and its active principle curcumin on T3-induced oxidative stress and hyperplasia in rat kidney. The study showed that turmeric exhibited better potential in comparison to curcumin in reversing thyroid hormone (T3) induced oxidative stress and hyperplasia in Wistar rats. It was hypothesised that regulation of cell cycle in rat kidney by T(3) is via reactive oxygen species and curcumin reverses the changes by scavenging them. Although the response trends are comparable for both turmeric and curcumin, the magnitude of alteration is more in the latter. Turmeric in the current dose schedule is a safer bet than curcumin in normalizing the T(3)-induced hyperplasia which may be due to the lower concentration of the active principle in the whole spice.[57]

It should be noted that in a 2008 study the aqueous extract of fresh rhizomes showed higher antioxidant properties as compared to the extracts from dry rhizomes, while the commercially available dry turmeric powder, commonly sold and used as a spice, has the least antioxidant properties. There was substantial loss of antioxidant properties when turmeric rhizomes are turned into a dry marketable powder.[58]

Neuroprotective activity: The therapeutic potential of turmeric in Alzheimer's disease (AD) was reviewed in a 2012 Pakistani study. AD is the most common form of dementia. There is limited choice in modern therapeutics and drugs available have limited success, with multiple side effects, in addition to high cost. Hence, newer and alternate treatment options are being explored for effective and safer therapeutic targets to address AD. Turmeric possesses multiple medicinal uses including treatment for AD. Curcuminoids, a mixture of curcumin, demethoxycurcumin, and bisdemethoxycurcumin, are vital constituents of turmeric. It is generally believed that curcumin is the most important constituent of the curcuminoid mixture that contributes to the pharmacological profile of parent curcuminoid mixture or turmeric. A careful literature study reveals that the other two constituents of the curcuminoid mixture also contribute significantly to the effectiveness of curcuminoids in AD. Therefore, it is emphasised in this review that each component of the curcuminoid mixture plays a distinct role in making the curcuminoid mixture useful in AD, and hence, the curcuminoid mixture represents turmeric in its medicinal value better than curcumin alone. The progress in understanding the disease aetiology demands a multiple- site-targeted therapy, and the curcuminoid mixture of all components, each with different merits, makes this mixture more promising in combating the challenging disease.[59]

The findings of an in vivo study revealed that optimised turmeric extract HSS-888 represents an important step in botanical based therapies for Alzheimer's disease by inhibiting or improving plaque burden, Tau phosphorylation (characteristic feature of Alzheimer's disease) and microglial inflammation leading to neuronal toxicity. In a previous in vitro study, the standardised turmeric extract, HSS-888, showed strong inhibition of beta amyloid aggregation and secretion in vitro, indicating that HSS-888 might be therapeutically important.[60]

Multiple pathways including oxidative stress and mitochondrial damage are implicated in neurodegeneration during

Parkinson's disease. The current Parkinson's disease drugs provide only symptomatic relief and have limitations in terms of adverse effects and inability to prevent neurodegeneration. Therefore, there is a demand for novel compound(s)/products that could target multiple pathways and protect the dying midbrain dopaminergic neurons, with potential utility as adjunctive therapy along with conventional drugs. To explore the neuroprotective property of turmeric in Parkinson's disease, mice were subjected to dietary supplementation with aqueous suspensions of turmeric for three months, mimicking its chronic consumption and challenged in vivo with 1-methyl- 4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). It was found that chronic dietary consumption of turmeric protects the brain against neurotoxic insults, with potential application in neurodegeneration.[61]

Cancer: Turmeric has been most widely investigated for its anticancer activity and has exhibited anticancer activity in human subjects. The most common cancer types in which turmeric has shown potential are those of the liver, breast, mouth and stomach.

In spite of major advances in oncology, the World Health Organization predicts that cancer incidence will double within the next two decades. Although it is well understood that cancer is a hyperproliferative disorder mediated through dysregulation of multiple cell signalling pathways, most cancer drug development remains focused on modulation of specific targets, mostly one at a time, with agents referred to as "targeted therapies," "smart drugs," or "magic bullets." How many cancer targets there are is not known, and how many targets must be attacked to control cancer growth is not well understood. Although more than 90% of cancer-linked deaths are due to metastasis of the tumour to vital organs, most drug targeting is focused on killing the primary tumour. Besides lacking specificity, the targeted drugs induce toxicity and side effects that sometimes are greater problems than the disease itself. Furthermore, the cost of some of these drugs is so high that most people cannot afford them. Turmeric has potential anticancer properties and is known for its safety and low cost. It can selectively modulate multiple cell signalling pathways linked to inflammation and to survival, growth, invasion, angiogenesis, and metastasis of cancer cells.[62]

Nitric oxide (NO) is involved in different stages of malignancies. Increased levels of NO have been reported in different leukaemias, including chronic myeloid leukaemia (CML) for which imatinib is the preferred drug for treatment. A 2012 study evaluated the effects of turmeric powder in reducing NO levels in 50 CML patients. The CML patients were divided into two groups, group A receiving imatinib (400mg twice a day) alone and group B receiving turmeric powder (5g three times/day dissolved in 150ml of milk) along with imatinib (400mg twice a day) for six weeks. Nitric oxide levels were estimated in these patients before and after receiving therapy. Nitric oxide levels were found to be significantly decreased in both the groups, but more significantly in group B after receiving the respective treatments. The authors concluded that turmeric acts as an adjuvant to imatinib in decreasing the NO levels and may help in the treatment of CML patients.[63]

The incidence of cancer is significantly lower in regions where turmeric is heavily consumed.Lower cancer incidence attributed to turmeric was investigated by examining its effects on tumour cell proliferation, on pro- inflammatory transcription factors NF-κB and transcription factor 3 (STAT3), and on associated gene products. Turmeric is more potent in inhibiting colorectal cancer growth in comparison to curcumin using cell based studies as reported recently. Cell proliferation and cell cytotoxicity were measured by the MTT method, NF-κB activity by EMSA, protein expression by Western blot analysis, ROS generation by FACS analysis, and osteoclastogenesis by TRAP assay. Turmeric inhibited NF-κB activation and down- regulated NF-κB-regulated gene products linked to survival (Bcl-2, cFLIP, XIAP, and cIAP1), proliferation (cyclin

D1 and c-Myc), and metastasis (CXCR4) of cancer cells. The spice suppressed the activation of STAT3, and induced the death receptors (DR)4 and DR5. Turmeric enhanced the production of ROS, and suppressed the growth of tumour cell lines. Furthermore, turmeric sensitised the tumour cells to chemotherapeutic agents capecitabine and taxol. Turmeric was found to be more potent than pure curcumin for cell growth inhibition. Turmeric also inhibited NF-κB activation induced by RANKL that correlated with the suppression of osteoclastogenesis. The results indicated that turmeric can effectively block the proliferation of tumour cells through the suppression of NF-κB and STAT3 pathways.[64]

An ethanolic extract of turmeric was found to produce remarkable symptomatic relief in patients with external cancerous lesions. Reduction in smell was noted in 90% of the cases and reduction in itching in almost all cases. Dry lesions were observed in 70% of the cases and a small number of patients (10%) had a reduction in lesion size and pain. In many patients the effect continued for several months. An adverse reaction was noticed in only one of the 62 patients evaluated.65 Turmeric extract offered protection against benzo[a] pyrene induced increases in micronuclei in circulating lymphocytes of healthy patients. In subsequent studies, patients suffering from oral submucous fibrosis (a highly potent pre-cancerous disease of the oral cavity mainly caused by chewing betal nut or tobacco.) were given a total oral dose of 3 g turmeric extract a day as a control for three months. Turmeric extract decreased the number of micronucleated cells both in exfoliated oral mucosal cells and in circulating lymphocytes.[66]

The superior toxicity of turmeric, in comparison to curcumin, against pancreatic cancer cells was shown in a study investigating the cytotoxic effects of turmeric force (TF), a supercritical and hydroethanolic extract of turmeric, alone and in combination with gemcitabine in two pancreatic carcinoma cell lines (BxPC3 and Panc-1). Gemcitabine is a first line cancer drug widely used for the treatment of pancreatic cancer. However, its therapeutic efficiency is significantly limited by resistance of pancreatic cancer cells to this and other chemotherapeutic drugs. TF was highly cytotoxic to the BxPC3 and Panc-1 cell lines, with IC50 values (the half maximal inhibitory concentration (IC50) is a measure of the effectiveness of a compound in inhibiting biological or biochemical function) of 1.0 and 1.22 microg/ml, respectively, and had cytotoxicity superior to that of curcumin. Gemcitabine IC50 value for both of these cell lines is 0.03 microg/ml; however, 30-48% of the pancreatic cancer cells are resistant to gemcitabine even at concentrations >100 microg/ml. In comparison, TF induced cell death in 96% of the cells at 50 microg/ml. The combination of gemcitabine and TF was synergistic with IC90 levels achieved in both pancreatic cancer cell lines at lower concentrations than for either agent alone. The synergistic effect was associated with an increased inhibitory effect of the combination on nuclear factor-kappaB activity and signal transducers and activators of STAT3 activities as compared to the single agent.[67]

Other studies: using rat models have shown the potential of turmeric against hepatocarcinogenisis and liver carcinogenisis.68,69 Hamster studies have shown that turmeric exhibits activity against oral carcinogenisis.[70]

A recent in vitro study has shown an ethanolic extract of turmeric can down-regulate a protein molecule (SIRT1) involved in longevity and diverse metabolic processes, including cancer.[71]

Antiproliferative activity: Studies over the past several years have indicated the growth inhibitory effects of turmeric against numerous cancer cells.

A 2013 in vitro study indicates that the use of turmeric extract might be a safer approach to finding a lasting cure for acute monocytic leukemia

(AML M5 or AMoL). AMol is one of the several types of leukemia that are still awaiting cures. The use of chemotherapy for cancer management can be harmful to normal cells in the vicinity of the target leukemia cells. This study assessed the potency of the extracts from lesser galangal, turmeric, and ginger against AML M5 to use the suitable fractions in neutraceuticals. Aqueous and organic solvent extracts from the leaves and rhizomes of lesser galangal and turmeric, and from the rhizomes only of ginger were examined for their antiproliferative activities against THP-1 AMoL cells in vitro. Lesser galangal leaf extracts in organic solvents of methanol, chloroform, and dichloromethane maintained distinctive antiproliferative activities over a 48-h period. The turmeric leaf and rhizome extracts and ginger rhizome extracts in methanol also showed distinctive anticancer activities. Further investigations will be required to establish the discriminatory tolerance of normal cells to these extracts, and to identify the compounds in these extracts that possess the antiproliferative activities.[72]

Turmeric extract inhibited the cell growth in Chinese hamster ovary cells at a concentration of 0.4 mg/ml and was cytotoxic to lymphocytes and Dalton's lymphoma cells at the same concentration when the anticancer activity of the rhizomes of turmeric were evaluated. Initial experiments indicated that turmeric extract and curcumin reduced the development of animal tumours.[73]

Chemoprevention: An in vivo study designed to seek the chemopreventive effects of turmeric and its mechanisms suggests that it can have beneficial effects on the early and late stages of liver pathogenesis, preventing and delaying liver carcinogenesis in mice. Unlike other forms of hepatocellular carcinoma, hepatocellular carcinoma induced by hepatitis B virus infection shows a poor prognosis after conventional therapies. Hepatitis B virus induces liver cirrhosis and hepatocellular carcinoma. Many researchers have made efforts to find new substances that suppress the activity of hepatitis B virus. Turmeric mixture concentrated with dextrose water by boiling was lyophilised. Turmeric treated mice showed less visceral fat, a smaller liver/body weight ratio and delayed liver pathogenesis. The authors suggest that turmeric should be considered as a potential chemopreventive agent for hepatitis B virus -related hepatocarcinogenesis.[74]

The modulating effects of turmeric, ethanolic turmeric extract and curcumin-free aqueous turmeric extract on the initiation or post-initiation phases of DMBA-induced mammary tumourigenesis were investigated in rats. The data clearly indicated that dietary administration of turmeric and ethanolic turmeric extract showed strong chemopreventive activity during initiation as well as post-initiation phases of DMBA-induced rat mammary tumourigenesis.[75]

A study aimed at assessing the potential chemopreventive effects of turmeric in hepatocarcinogenic rats has shown that dietary supplementation of turmeric delayed the initiation of carcinogenesis.76 Turmeric was shown to inhibit promotion of lymphoma cells induced by 12-O-tetradecanoylphorbol-13-acetate (TPA) in in vitro studies evaluating natural products as potential cancer chemopreventive agents.[77]

Antimutagenic: A study on the anti-mutagenic effects of turmeric were assessed in 16 chronic smokers. It was observed that turmeric, given in doses of 1.5 g/day for 30 days, significantly reduced the urinary excretion of mutagens in smokers. In contrast, in six non-smokers, who served as control, there was no change in the urinary excretion of mutagens after 30 days. These results indicate that dietary turmeric is an effective anti-mutagen and it may be useful in chemoprevention. Randomised, placebo controlled studies are required to confirm these findings.[78]

Turmeric has been shown to inhibit chemical carcinogenesis. Curcumin free aqueous

turmeric, and to a lesser degree ethanolic turmeric extract and turmeric powder, have the potential to suppress benzo(a)pyrene- induced forestomach tumours in mice.[79]

In a similar study, the antitumour activity of turmeric was investigated in mice by comparing the activities of an aqueous turmeric extract and its constituents, a curcumin-free aqueous turmeric extract and curcumin on chemical carcinogenesis. Both the aqueous extract and the curcumin-free extract dose dependently exhibited antimutagenic activity against bacteria. Furthermore, the incidence and multiplicity of forestomach tumours induced by benzo [alpha]pyrene in the mice were significantly inhibited.[80]

In an in vitro study, turmeric was shown to be as effective as rosemary in decreasing the levels of heterocyclic amines (mutagenic compounds formed when foods are cooked at high temperatures) in fried beef patties.[81]

Immunomodulation: A recent in vitro study using hot water turmeric extract has shown that it exhibits immune stimulatory activities in human peripheral blood mononuclear cells. The findings revealed the potential use of turmeric crude extract as an adjuvant supplement for cancer patients, whose immune activities were suppressed during chemotherapies.[82]

Radioprotective: A study investigated the effect of an aqueous extract of turmeric on the sensitivity of Escherichia coli, Bacillus megaterium and Bacillus pumilusspores spores to gamma radiation. The extract offered protection to these organisms against inactivation by gamma-radiation. The study indicated the importance of turmeric, among ingredients in food, as a dose-modifying factor during radiation processing.83 Another study investigated the possible role of crude turmeric extracts in radioprotection by a variety of methods. This study revealed that dimethyl sulfoxide extracts of turmeric produced a significant amount of radioprotection, which is very similar in nature and extent to that imparted by curcumin. Turmeric also clearly showed protection against X-ray induced DNA damage of E. coli cells.[84]

Gastrointestinal effects: Hepatoprotective

A 2013 clinical trial has shed light on turmeric's remarkable liver protective and regenerative properties. Previously, the hepatoprotective activity of turmeric and its constituents have been reported in the literature. Recent evidence has shown that turmeric, or curcumin, can improve the liver function in rats with hepatic injury.[85,86,87,88] In view of the hepatoprotective and other beneficial effects of fermented turmeric powder (FTP) in animal models, a randomised, double-blind, placebo-controlled clinical trial was designed and conducted to evaluate the effects of 12-week FTP treatment on serum aminotransferase levels in subjects with elevated alanine transaminase (ALT) levels. The hypothesis tested was that FTP might improve liver function. Therefore, serum ALT levels was defined as the primary end point of the study. The trial was conducted between November 2010 and April 2012 at the clinical trial centre for functional foods of the Chonbuk National University Hospital, South Korea. The data from this trial indicates that FTP is effective and safe, generally well-tolerated without severe adverse effects (AEs), in the treatment of subjects with elevated ALT levels over a 12 weeks period. The FTP was crushed turmeric which had been fermented with 2% (wt/wt) of Aspergillus oryzae at 25°C for 36 h and dried. Fermented turmeric was standardised to 0.79 mg curcumin per 1.0 g powder. Average curcumin contents in non-fermented turmeric and FTP were approximately 2.0 mg/g and 0.79 mg/g, respectively. In this study, the subjects were not actively asked to change their lifestyle or to change their diet. The trial included 60 subjects, 20 years old and above, who were diagnosed

with mild to moderate elevated ALT levels between 40 IU/L and 200 IU/L. Sixty subjects were randomised to receive FTP 3.0 g per day or placebo 3.0 g per day for 12 weeks.

The treatment group received two capsules of FTP three times a day after meals, for 12 weeks. The primary efficacy endpoint was change in the ALT levels in the two groups. The secondary efficacy endpoints included its effect on aspartate aminotransferase (AST), gamma- glutamyl transferase (GGT), total bilirubin (TB), and lipid profiles. Safety was assessed throughout the study using ongoing laboratory tests. Sixty subjects were randomised in the study (30 into the FTP group, 30 into the placebo group), and among them, twelve subjects were excluded from the analysis for protocol violation, adverse events or consent withdrawal. The two groups did not differ in base line characteristics. After 12 weeks of treatment, 48 subjects were evaluated. Of the 48 subjects, 26 randomly received FTP capsules and 22 received placebo. The FTP group showed a significant reduction in ALT levels after 12 weeks of treatment compared with the placebo group ($p = 0.019$). It was also observed that the serum AST levels were significantly reduce in the FTP group than placebo group ($p = 0.02$). The GGT levels showed a tendency to decrease, while the serum alkaline phosphatase (ALP), TB, and lipids levels were not modified. There were no reported severe AEs during this study, or abnormalities observed on blood glucose, total protein, albumin, blood urea nitrogen (BUN), and creatinine levels.[89]

Anti-ulcer activity: doctors used pills “Khamin Chan (Turmeric)” powder mixed with honey to successfully cure their ailment. The authors were interested in proving the effects of turmeric on the epithelial mucosa of stomach and duodenum of peptic ulcer patients to see whether the healing of the ulcer in the mucosa by endoscopy corresponds to the disappearance of abdominal pain.[90] An oral extract of turmeric was found to protect the gastric mucosal layer of pylorus ligated rats in a dose dependent manner and was as effective as ranitidine at higher doses of turmeric. Turmeric specifically inhibited gastric acid secretion by blocking H(2) histamine receptors in a competitive manner.[91]

Irritable Bowel Syndrome: In a partially blinded, randomised, two-dose, pilot study it was shown that turmeric may help reduce irritable bowel syndrome (IBS) symptomology. The study was not placebo- controlled and the authors acknowledged that a placebo effect was likely to have contributed to positive results. Five hundred (500) volunteers were screened for IBS using the Rome II criteria. Two hundred and seven (207) suitable volunteers were randomised. One or two tablets of a standardised turmeric extract (72 or 144mg) were taken daily for eight weeks. A statistically significant reduction in IBS prevalence compared with baseline was seen in both treatment groups (53% and 60% with the 72mg and 144mg doses, respectively). A self-reported improvement in symptoms (67% and 70%) and increased quality of life (assessed by questionnaire) was also reported.[92] Another study hypothesised that turmeric in curry might increase bowel motility and activate hydrogen-producing bacterial flora in the colon, thereby increasing the concentration of breath hydrogen. Eight healthy subjects fasted for 12 hours and ingested curry and rice with or without turmeric. Breath-hydrogen concentrations were analysed every 15 minutes for six hours by gas chromatography with a semiconductor detector. Curry with turmeric significantly increased the area under the curve of breath hydrogen and shortened small-bowel transit time, compared with curry not containing turmeric. These results suggested that dietary turmeric activated bowel motility and carbohydrate colonic fermentation.[93]

Dypepsia: A multicenter, randomised, double-blind placebo-controlled trial investigating the efficacy of turmeric for treatment of dyspepsia and flatulence in 116 adult patients who had acid dyspepsia, flatulent dyspepsia or atonic dyspepsia found that 87% of patients receiving turmeric

responded to the treatment compared to 53% receiving placebo. Each patient received two capsules of placebo or study drugs four times a day for a week. The differences in efficacy between placebo and active drugs were statistically significant and clinically important.[94]

Chologogue and hypolipidaemic: A recent animal study has found that turmeric may be considered a functional food for regulating plasma. An open, pilot study (phase II clinical trial) on the effect of turmeric on healing peptic ulcers showed a satisfactory reduction in abdominal pain and discomfort in the first week of a four week treatment. Forty-five patients (24 men and 21 women, aged between 16-60 years) were included in the study. Of these, 25 patients (18 men and 7 women) underwent endoscopy for their ulcers located in the duodenal bulb and gastric angulus (the angulus being defined as the lowest point of the lesser curvature). The ulcer sizes varied between 0.5 to 1.5 cm in diameter. Turmeric-filled capsules (crude powder of the dried rhizome) was given orally in the dose of two capsules (300 mg each) five times daily, one half to an hour before meals, at 16.00 hours and at bedtime continuously. The result after four weeks of treatment showed that ulcers were absent in 12 cases (48%). Eighteen cases (72%) had no ulcers after eight weeks of treatment and 19 cases (76%) did not have ulcers after 12 weeks of treatment. The remaining 20 cases were not found to have ulcers and some did not undergo endoscopy. These 20 people appeared to have erosions, gastritis and dyspepsia, and turmeric capsules were given to these people for four weeks. The abdominal pain and discomfort satisfactorily subsided in the first and second weeks. The authors concluded that turmeric has the capacity to heal peptic ulcers. To study the side effects of turmeric, blood chemistry and haematology were performed. All 54 patients had no significant changes in haematological system, liver and renal functions both before and after treatment. The authors wrote that many Thai people suffer from abdominal pain due to gastric and duodenal ulcers. Traditional cholesterol levels and preventing the development of fatty liver in people who frequently consume a high- cholesterol diet. The results showed that rats fed a high- cholesterol diet supplemented with turmeric extract had a significant increase in high density lipoprotein (HDL) cholesterol and decreases in total plasma cholesterol and low density lipoprotein (LDL) cholesterol along with several other variables, showing that turmeric prevents hypercholesterolaemia and the formation of fatty liver by the modulation of expressions of enzymes that are important to cholesterol metabolism.[95]

Anti-atherogenic activity: Atherosclerosis is characterised by oxidative damage that affects lipoproteins, the walls of blood vessels and subcellular membranes. The oxidation of LDL also plays an important role in its development.[96]

A study was done evaluating the effects of oral supplementation with a turmeric ethanol and aqueous extract on the susceptibility to oxidation of cellular, and subcellular, membranes affected in the atherosclerotic process, such as erythrocyte membranes and liver microsomes, in rabbits fed with a high-fat diet. The results show that turmeric inhibits erythrocyte and liver microsome membrane oxidation and may contribute to the prevention of effects caused by a diet high in fat and cholesterol in blood and liver during the development of atherosclerosis.[97] In another study oral administration of turmeric extract inhibited LDL oxidation and had hypocholesterolaemic effects in atherosclerotic rats.[98]

Wound healing: The potential efficacy of fresh turmeric paste to heal wounds was tested in a preclinical animal study. Turmeric paste was compared with honey as a topical medicament against a control on experimentally created full-thickness circular wounds in 18 rabbits. Wound healing was assessed on the basis of physical, histomorphological, and histochemical parameters on treatment days 0, 3, 7, and 14. Only tensile strength

was measured on day 14 of treatment. It was observed that the wound healing was statistically significantly faster in both treatment groups compared to the control group.[99]

Analgesic activity: A double-blind randomised placebo-controlled study found turmeric improved postoperative pain and fatigue in 50 patients following laparoscopic cholecystectomy.[100]

Antimicrobial activity: Turmeric has been shown to inhibit the growth of numerous microorganisms including bacteria, viruses and fungi. An in vitro study using a methanol extract of the dried powdered turmeric rhizome inhibited the growth of Helicobacter pylori, a Group 1 carcinogen associated with the development of gastric and colon cancer.[101] An aqueous solution of turmeric extract was shown to preserve and extend the shelf life of vacuum- packaged rainbow trout by retarding microbial growth.[102] Histamine producing bacteria (Vibrio parahaemolyticus, Bacillus cereus and Proteus mirabilis) were inhibited by turmeric at 5% concentration. Another study reported the bactericidal activities of turmeric tuber extract and powder against Escherichia coli BL-21 strain.[104]

Antiviral activity: A recent in vitro study showed that an aqueous extract of turmeric repressed hepatitis B virus replication through enhancing the level of p53 protein. The authors concluded that turmeric can be used as a safe and specific drug for patients with liver diseases caused by HBV infection. In addition, turmeric did not have any cytotoxic effects on liver cells.[105]

Antifungal activity: A crude ethanolic extract of turmeric exhibited an inhibition zone range of 6.1 to 26.0 mm when tested for antifungal activity by agar disc diffusion method against 29 clinical strains of dermatophytes.[106] The ethanolic extract of turmeric also exhibited excellent (100%) phytotoxic activity against Lemma minor. It was also found to possess good antifungal activities against Trichophyton longifusus (65%).[107]

Other actions: Nephroprotective. End-stage renal disease (ESRD) due to type 2 diabetic nephropathy is a very common condition which is increasing in prevalence, and is associated with high global levels of mortality and morbidity. Both proteinuria and transforming growth factor-β (TGF-β) may contribute to the development of ESRD in patients with diabetic nephropathy. Experimental studies indicate that turmeric improves diabetic nephropathy by suppressing TGF-β. A randomised, double-blind and placebo-controlled study in Iran investigated the effects of turmeric on serum and urinary TGF-β, interleukin-8 (IL-8) and tumour necrosis factor-α (TNF-α), as well as proteinuria, in patients with overt type 2 diabetic nephropathy.

The study consisted of 40 patients with overt type 2 diabetic nephropathy that were randomly assigned to either the trial group (n = 20) and a control group (n = 20). Each patient in the trial group received one capsule with each meal containing 500 mg turmeric, of which 22.1 mg was the active ingredient curcumin (three capsules daily) for two months. The control group received three capsules identical in colour and size containing starch for the same 2 months. Serum levels of TGF-β and IL-8 and urinary protein excretion and IL-8 decreased significantly comparing the pre- and post-turmeric supplementation values. No adverse effects related to turmeric supplementation were observed during the trial. The authors of this study concluded that short-term turmeric supplementation can attenuate proteinuria, TGF-β and IL-8 in patients with overt type 2 diabetic nephropathy and can be administered as a safe adjuvant therapy for these patients.[108]

A Swedish study examined the effects of turmeric on postprandial plasma glucose, insulin levels and glycemic index in healthy subjects.

Fourteen healthy subjects were assessed in a crossover trial. A standard 75 g oral glucose tolerance test (OGTT) was administered together with capsules containing a placebo or turmeric. Finger- prick capillary and venous blood samples were collected before and 15, 30, 45, 60, 90, and 120 min after the start of the OGTT to measure the glucose and insulin levels, respectively. The study found that the ingestion of 6 g of turmeric increased postprandial serum insulin levels but had no effect on plasma glucose levels or glycemic index in these healthy subjects. The results indicate that turmeric may have an effect on insulin secretion.[109]

Turmeric has shown potential against diabetes in numerous animal models and in vitro studies. A study using mice has shown that turmeric is a promising ingredient of functional food for the prevention and/ or amelioration of type 2 diabetes and that curcumin, demethoxycurcumin, bisdemethoxycurcumin, and ar- turmerone mainly contribute to the effects via PPAR-gamma activation. Turmeric extract significantly suppressed an increase in blood glucose level in type 2 diabetic mice.[110]

Another study aimed at comparing the modulatory effects of turmeric against diabetes and oxidative stress induced by streptozotocin and nicotinamide in rats. The results proved that turmeric significantly alleviates signs of diabetes (hyperglycaemia and dyslipidaemia) and elevations in atherogenic indices and cellular toxicity in the rats by increasing the production of insulin, enhancing the antioxidant defence system and decreasing lipid peroxidation.111 Another rat study indicated that turmeric is effective against the development of diabetic cataract.[112]

A study dealing with the effects of freeze dried rhizome powder of turmeric dissolved in milk on normal as well as diabetic rat models. Diabetes of type II and type I was within 3 days of a single administration of doses of 45 and 65 mg kg−1 of streptozotocin respectively. Various parameters such as blood glucose levels, triglycerides (TG), total cholesterol (TC), high density lipoprotein (HDL), very low density lipoprotein (VLDL), low density lipoprotein (LDL), serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvate transaminase (SGPT), alkaline phosphatise (ALP), creatinine, haemoglobin (Hb), urine protein and urine sugar in addition to body weight (bw) were taken into consideration and were analysed after administration of variable doses of rhizome powder. The dose of 200 mg kg−1 was identified as the most effective dose as it increased HDL, Hb and bw ($p<0.05$) with significant decrease in the levels of blood glucose, lipid profile and hepatoprotective enzymes ($p<0.001$).[113]

An aqueous extract of turmeric was shown to have insulin releasing action in an in vitro study investigating its effect on tissues involved in glucose homeostasis. The extract was prepared by soaking 100 g of ground turmeric in 1 L of water, which was filtered and stored at -20°C prior to use.[114]

An aqueous extract of turmeric has been shown to inhibit human pancreatic amylase activity in an in vitro study. This action thereby reduces the rate of starch hydrolysis leading to lowered glucose levels.[115]

Turmeric extract was shown to have a strong recovery effect (greater than 20%) on cisplatin-induced nephrotoxicity in an in vitro test. It was suggested that additional studies should be conducted to determine if turmeric possesses novel therapeutic agents that can be used for the prevention or treatment of renal disorders.[116]

Antidepressant: A recent animal study suggests that turmeric has antidepressant properties and may be a useful agent against depression. The study was undertaken to determine the behavioural, neurochemical and neuroendocrine effects of the ethanolic extract of turmeric using the forced swimming test (FST) in mice. The results suggested that antidepressant properties of the ethanolic extract of turmeric were mediated through regulations of neurochemical and neuroendocrine systems.[117]

An earlier study demonstrated that aqueous extracts of turmeric had specifically antidepressant effects in vivo. The results showed that activity of turmeric in depression may be mediated in part through monoamine oxidize A inhibition in mouse brains.[118]

Antiageing: A study aiming to clarify whether turmeric prevents chronic ultraviolet B (UVB)-irradiated skin damage in mice has had positive results. The effects of a turmeric extract on skin damage including changes in skin thickness and elasticity, pigmentation and wrinkling caused by long-term, low-dose ultraviolet B irradiation in melanin-possessing hairless mice were studied. The extract (at 300 or 1000 mg/kg, twice daily) prevented an increase in skin thickness and a reduction in skin elasticity induced by chronic UVB exposure. It also prevented the formation of wrinkles and melanin (at 1000 mg/kg, twice daily) as well as increases in the diameter and length of skin blood vessels and in the expression of matrix metalloproteinase-2 (MMP-2). Prevention of UVB-induced skin aging by turmeric may be due to the inhibition of increases in MMP-2 expression caused by chronic irradiation.[119]

An animal study has suggested enhanced learning ability, and spatial memory, after turmeric extract treatment.[120]

Protection against chemical insults: Several animal studies have shown that turmeric can protect the normal cells, tissues and organs against the damage caused by external insults including reducing arsenic and fluoride toxicity, and carbon tetrachloride induced hepatotoxicity.[121,122,123]

Larvicidal and insecticidal activity: The results of a 2012 study show that at turmeric may serve as a natural larvicidal agent. A hydrodistillate extract of turmeric demonstrated larvicidal activity against the dengue vector Aedes aegypti, the yellow fever mosquito. Early instar larvae were more susceptible to the extract than the late instar larvae and pupae.[124]

The essential oil of turmeric was found to be insectidal in an Indian study. The study investigated the contact and fumigant toxicity of turmeric and its effect on progeny production in three stored-product beetles, Rhyzopertha dominica F. (lesser grain borer), Sitophilus oryzae L. (rice weevil), and Tribolium castaneum Herbst (red flour beetle). The oil was insecticidal in both contact and fumigant toxicity assays.[125]

Indications: Adjunctive cancer treatment, chemoprevention (to reverse, suppress or prevent the development of cancer) and chemosensitisation (makes tumour cells more sensitive to chemotherapy). Inflammatory conditions such as arthritis, osteoarthritis, irritable bowel sydrome (IBS), inflammatory bowel disease, asthma, eczema, psoriasis, lupus nephritis. Cardiovascular disease prophylaxis, Dyspepsia, peptic ulcer, Liver dysfunction, Infections, Adjunct in the treatment of hyperlipidaemia (abnormally elevated levels of any or all lipids and/or lipoproteins in the blood. Primary hyperlipidemia is usually due to genetic causes (such as a mutation in a receptor protein), while secondary hyperlipidemia arises due to other underlying causes such as diabetes.

Lipid and lipoprotein abnormalities are common in the general population, and are regarded as a modifiable risk factor for cardiovascular disease due to their influence on atherosclerosis.), Adjunctive diabetes treatment, Topically for skin conditions, sprains and strains, adjunct in periodontitis.

Toxicity: Based on historical use, turmeric is generally considered safe when used in amounts commonly found in foods.126 The US Food and Drug Administration (FDA) has granted turmeric, turmeric extract and turmeric oleoresin Generally Recognised as Safe (GRAS) status.[127]

Use in Pregnancy: Safety during pregnancy and lactation has not been established. In the absence of sufficient data the use of turmeric during pregnancy and lactation is not recommended.[128] When used as a spice this herb is most likely to be safe.[129]

Contraindications: It is contraindicated in patients with obstruction of the bile duct and should be used only after seeking professional advice if gallstones are present.130 Contraindicated when used in patients allergic to turmeric, any of its constituents (including curcumin), certain yellow food colourings or other members of the Zingiberaceae (ginger) family.[131]

Drug Interactions: None reported. The potential for preparations of turmeric to interact with other medicines concurrently, particularly those with similar or opposing effects, should be considered.[132,133]

Remedy recipes: Wound paste. To make a paste for wounds: put 30g dried turmeric powder in a pan with 150ml water and simmer to a thick paste. Place gauze on affected area and apply the paste for a few minutes, 3 times a day.

Golden milk. Combine 200ml milk, 1⁄2 tsp turmeric paste (see above), 1 tsp almond oil and honey (to taste) in a pan. Heat to just below boiling point. Then whizz in a blender to froth (adding fruit such as bananas and berries, if liked).[134]

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