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AN EXAMINATION OF THE INFLUENCE OF CURCUMIN ON HUMAN HEALTH

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Abstract:

The fact that turmeric is the primary source of the polyphenol curcumin makes it of interest to people in the medical and scientific communities as well as those who have a passion for cooking. Turmeric has been known for a long time to possess curative qualities. It is helpful in the therapy of illnesses related to oxidative stress and inflammation, as well as metabolic syndrome, arthritis, anxiety, and high cholesterol. It is also possible that it may aid in the control of inflammation and muscular soreness brought on by exercise, hence improving recovery and performance in persons who are active. In addition, those who do not have identified health concerns may reap the advantages of taking a very moderate amount of the complex and still have positive effects on their health. The majority of these advantages may be traced back to the antioxidant and anti-inflammatory actions that it has. Consuming curcumin on its own does not result in the related health benefits owing to the compound's low bioavailability. This low bioavailability seems to be largely caused by poor absorption, quick metabolism, and rapid elimination. There are other factors that might contribute to an increase in bioavailability. For instance, piperine, which is the primary active component of black pepper, has been demonstrated to boost the bioavailability of curcumin by a factor of 2,000 when it is mixed in a complex with the compound. Multiple health advantages may be gained by using curcumin in combination with other medicines. This article's goal is to provide a condensed summary of the vast body of research that has been conducted on the positive effects that curcumin may have on one's health.

Keywords: curcumin; turmeric; antioxidant; anti-inflammatory; polyphenol

Introduction:

Both the culinary and the medical/scientific communities have shown a significant amount of interest in turmeric as a spice due to its purported health benefits. [1] Curcuma longa, sometimes known as turmeric, is a rhizomatous herbaceous perennial plant that is a member of the ginger family. Curcumin comes from turmeric, which has been used for therapeutic purposes for thousands of years. However, researchers have only recently been able to pinpoint the specific mechanism(s) of action and the bioactive components of curcumin [2]. Curcumin (1,7-bis(4-hydroxy-3-

methoxyphenyl)-1,6-heptadiene-3,5-dione), which is also known as diferuloylmethane, is the primary naturally occurring polyphenol that can be found in the rhizome of Curcuma longa (turmeric) and in other Curcuma spp. [3]. [Curcuma longa] is a species of the Curcuma genus In many Asian nations, curcuma longa has a long history of usage as a medicinal plant owing to its antioxidant, anti-inflammatory, antimutagenic, antibacterial, and anticancer [7,8] characteristics. [4] [5] [6] [7] [8] [9] [10] [11] [12] [13] [14] [15] [16].

The polyphenol curcumin has been demonstrated to target many signalling molecules in addition to displaying action at the cellular level, which helps to support the numerous health advantages that it has [2]. It has been shown to be beneficial for disorders characterised by inflammation [9], metabolic syndrome [10], and pain [11], as well as beneficial for the therapy of inflammatory and degenerative eye problems [12,13]. [9], [10], and [11] In addition to this, there is evidence that it is beneficial to the kidneys [14]. The majority of the therapeutic advantages attributed to taking curcumin are caused by its antioxidant and anti-inflammatory actions [2,9]. This is despite the fact that curcumin seems to have a plethora of other benefits. Ingestion of curcumin by itself is associated with a number of significant drawbacks, one of the most significant of which is its poor bioavailability [15], which appears to be primarily caused by poor absorption, rapid metabolism, and rapid elimination. This is the case despite the fact that curcumin is said to be beneficial via inflammatory and antioxidant mechanisms. By targeting each of these distinct processes, many compounds have been investigated for their potential to increase the bioavailability of curcumin. The majority of them have been created with the goal of inhibiting the metabolic route of curcumin, which will result in an increase in the compound's bioavailability. For instance, piperine, which is a recognised bioavailability enhancer and is the primary active component of black pepper [16], has been related with a boost in the bioavailability of curcumin that is equivalent to a factor of 2,000 [17]. Therefore, it would seem that the problem of low bioavailability may be remedied by adding substances like piperine that promote bioavailability, so producing a curcumin complex.

Curcumin is becoming more popular and is utilised all over the globe in a broad variety of applications due to its vast range of possible health advantages. For instance, turmeric, which contains curcumin, has been used in the preparation of curries in India; in Japan, it is served in

tea; in Thailand, it is used in cosmetics; in China, it is used as a colourant; in Korea, it is served in drinks; in Malaysia, it is used as an antiseptic; in Pakistan, it is used as an anti-inflammatory agent; and in the United States, it is used in mustard sauce, cheese, butter, and chips, as a preserv You may get curcumin in a variety of forms, such as capsules, pills, ointments, energy drinks, soaps, and cosmetics [2]. Good tolerability and safety profiles have been shown by clinical trials, even at doses between 4000 and 8000 mg/day [18] and of doses up to 12,000 mg/day of 95 percent concentration of three curcuminoids: curcumin, bisdemethoxycurcumin, and demethoxycurcumin [19]. Curcuminoids have been approved by the Food and Drug Administration (FDA) of the United States as "Generally Recognized As Safe" (GRAS) [2].

This article's goal is to offer a concise summary of the vast body of research that has been conducted on the possible positive effects that curcumin may have on one's health. Because there is such a large body of research on the subject of cancer and other disease states, we have decided not to conduct a literature review on those topics but rather to concentrate on the benefits associated with certain common health conditions as well as the benefits that accrue to healthy people. Please refer to the article that was written by Kunnumakkara et al. in 2017 [20] for an in-depth analysis of the impact that curcumin has on cancer.

Mechanisms of Action:

Antioxidant:

Curcumin's capabilities as an antioxidant and as an anti-inflammatory are the two principal mechanisms that explain the bulk of its benefits on the many illnesses included in this study [21,22]. It has been shown that curcumin is able to reduce systemic indicators of oxidative stress [23]. There is some evidence that it may be able to improve the serum activity of antioxidants such as superoxide dismutase (SOD) [24–26]. A recent systematic review and meta-analysis of randomised control data related to the efficacy of supplementation with purified curcuminoids on oxidative stress parameters—indicated a significant effect of curcuminoids supplementation on all investigated parameters of oxidative stress including plasma activities of SOD and catalase, as well as serum concentrations of glutathione peroxidase (GSH) and lipid peroxides [23]. This review and analysis indicated that curcuminoids supplementation has It is important to note that all of the studies that were included in the meta-analysis employed some kind of formulation in order to circumvent the

difficulties associated with bioavailability, and of those, four out of the six made use of piperine. The impact that curcumin has on free radicals is accomplished via a variety of distinct methods. It has the ability to scavenge various forms of free radicals, such as reactive oxygen and nitrogen species (ROS and RNS, respectively) [25]; it has the ability to modulate the activity of GSH, catalase, and SOD enzymes active in the neutralisation of free radicals [21,22]; and it has the ability to inhibit ROS-generating enzymes, such as lipoxygenase/cyclooxygenase and xanthine hydrogenas In addition, curcumin is a lipophilic molecule, which enables it to be an effective scavenger of peroxyl radicals; hence, much like vitamin E, curcumin is also regarded to be a chain-breaking antioxidant [27].

Anti-Inflammatory:

The pathological processes of oxidative stress and inflammation are strongly associated; in fact, one may be readily generated by the other. Oxidative stress has been linked to a number of chronic illnesses, and its pathological processes are closely related to those of inflammation. The fact that inflammatory cells release a lot of reactive species at the site of inflammation, which ultimately results in oxidative stress, is evidence of the connection between oxidative stress and inflammation [28]. In addition, the production of reactive oxygen and nitrogen species may kick off an intracellular signalling cascade, which in turn boosts the expression of genes involved in pro-inflammatory processes. [10,19,29,30] Numerous chronic illnesses and disorders have been linked to the presence of inflammation in its early stages of development. The Alzheimer's disease (AD), Parkinson's disease, multiple sclerosis, epilepsy, cerebral injury, cardiovascular disease, metabolic syndrome, cancer, allergy, asthma, bronchitis, colitis, arthritis, renal ischemia, psoriasis, diabetes, obesity, depression, fatigue, and acquired immune deficiency syndrome are some of the diseases that fall into this category. AIDS [10]. This impact is mediated by the activation of a transcription factor called nuclear factor (NF)-B, and tumour necrosis factor alpha, often known as TNF-alpha, is a significant mediator of inflammation that is present in the majority of illnesses. It is believed that TNF- is the most powerful activator of NF-B; however, NF-B is also responsible for controlling how much TNF- is produced in the body. In addition to TNF-, NF-B is activated by the majority of pro-inflammatory cytokines, gram-negative bacteria, a variety of disease-causing viruses, environmental pollutants, chemical, physical, mechanical, and

psychological stress, high glucose levels, fatty acids, ultraviolet radiation, cigarette smoke, and other factors that contribute to the development of disease. Therefore, medicines that downregulate NF-B as well as gene products that are controlled by NF-B have the potential to be effective against numerous of these disorders. It has been established that curcumin may inhibit the activation of NF-B, which can be brought on by a variety of inflammatory stimuli [10]. Curcumin has also been demonstrated to reduce inflammation via a variety of methods, some of which are outside the scope of this study; this finding lends credence to the theory that its mode of action makes it a candidate for the role of an anti-inflammatory drug [10].

Arthritis:

Osteoarthritis (OA), also known as degenerative joint disease, is an example of a disorder that may develop over time and is linked to inflammation of both a chronic and acute kind. It has a global prevalence of over 250 million individuals, resulting in greater expenditures for medical treatment, a reduction in the ability to carry out activities of daily living (ADL), and, ultimately, a worse quality of life [31,32]. Although osteoarthritis (OA) was once thought of primarily as a degenerative and non-inflammatory condition, it is now recognised as having inflammatory aspects, including elevated cytokine levels, as well as potentially being connected with systemic inflammation. This is a change from the previous perception of OA, which held that it did not have any inflammatory components. There is currently no known cure for the condition; however, there are a number of pharmacological treatments available. Many of these treatments are expensive and come with unwelcome side effects. As a result, there is a growing interest in alternative therapies such as nutritional supplements and natural medicines [35]. Curcumin's anti-arthritic properties in persons with osteoarthritis (OA) and rheumatoid arthritis (RA) have been shown in a number of research [36–39]. In a randomised, double-blind, placebo-controlled trial, forty participants with mild-to-moderate degree knee osteoarthritis were randomly assigned to receive either curcuminoid (500 mg/day in three divided doses; n = 19) with 5 mg piperine added to each 500-mg dose or a matched placebo (n = 21) for a period of six weeks. Both groups were given the same amount of piperine (5 mg added to each 500-mg dose). Scores on the visual analogue scale (VAS) decreased by a significantly greater amount (p 0.001), the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores decreased by a significant amount (p = 0.001), and

Lequesne's pain functional index (LPFI) scores decreased by a significant amount (p = 0.013) in the treatment group when compared to the placebo group. When the WOMAC subscales were compared, there were substantial improvements in the ratings for pain and physical function (p 0.001), but there were no changes in the score for stiffness. In addition, there was a reduction in systemic oxidative stress, which was evaluated by blood activities of SOD and concentrations of decreased GSH and malonedialdehyde (MDA), in participants getting the medication as compared to the subjects receiving the placebo [11]. There was no correlation seen between these improvements and shifts in the circulating cytokines. The authors speculate that the lack of changes in circulating cytokines, despite improvements in pain, may be due to the fact that in OA, inflammatory markers in the synovial fluid may be more likely to be elevated than systemic markers, whereas in RA, systemic markers may be more likely to be increased. This is in contrast to the possibility that in RA, systemic markers may be more likely to be increased. As a result, they propose that it is more possible that the positive benefits of curcuminoids in OA are due of the local anti-inflammatory effects rather than the systemic effects. In addition, it's possible that the amount of time spent taking the supplements wasn't sufficient. In a randomised controlled trial that lasted for a longer period of time (eight months), fifty people who had been diagnosed with OA were split into two groups. The first group received the standard treatment that was recommended by their doctor. The second group received the standard treatment as well as two 500 mg tablets per day that contained a natural curcuminoid mixture that contained phosphatidyl-choline (40 percent) and microcrystalline cellulose (40 percent). Scores on the WOMAC, physical function, and stiffness all went down considerably (p 0.05) in the group that received therapy when compared to the group that did not get treatment. In addition, when comparing baseline to follow-up, the treatment group demonstrated significant reductions in all inflammatory markers (soluble CD40 ligand (sCD40L), interleukin 1 beta (IL-1), interleukin 6 (IL-6), soluble vascular cell adhesion molecule 1 (sVCAM-1), and erythrocyte sedimentation rate (ESR), whereas the control group did not. The fact that both groups in this trial continued to receive conventional treatment means that the subject of whether or not supplementation with curcumin may be utilised instead of usual therapy such as nonsteroidal anti-inflammatory medications was not investigated (NSAIDS). 367 individuals with primary

knee osteoarthritis and a pain level of 5 or higher were randomly assigned to receive either ibuprofen 1200 mg/day or C. domestica extracts 1500 mg/day for a period of four weeks. The purpose of this study was to investigate this subject. When compared to the scores obtained at the beginning of the study, those obtained at weeks 0, 2, and 4 on the WOMAC indicated a substantial improvement in both groups. According to the results of the noninferiority test, the mean difference (95 percent confidence interval) of WOMAC total, WOMAC pain, and WOMAC function scores at week 4 adjusted by values at week 0 of C. domestica extracts were non-inferior to those for the ibuprofen group ($p = 0.010$, $p = 0.018$, and $p = 0.010$, respectively). This indicates that individuals who took curcumin and individuals who took The group who took the nonsteroidal anti-inflammatory drugs did have higher stomach problems. According to these findings, curcumin may provide an alternative to NSAIDS for individuals with OA who are seeking therapy but are suffering significant side effects [12]. This was corroborated by the findings of a pilot trial which demonstrated that a dosage of 2 grammes of curcumin had an analgesic effect in participants who were experiencing acute pain but did not have a diagnosis of OA. At this level, the activity was greater than that associated with 500 mg of acetaminophen, but a smaller dose (1.5 g, which is equivalent to 300 mg of curcumin) provided only temporary and sometimes insufficient relief from pain, which is suggestive of inferior therapeutic plasma concentrations. It took just two hours for the analgesic impact of the dosage to become significant, which is comparable to the time it took for acetaminophen to exert its effects. In contrast, the NSAID had a quicker onset of action, with patients reporting the greatest improvement in their pain level one hour after taking the medication. However, this was accompanied by a considerable worsening of their gastrointestinal symptoms. This lends credence to the usage of 2 grammes of curcumin (which is a greater dose than is required for inflammation) for the treatment of pain as a viable alternative to NSAIDS.

Metabolic Syndrome:

The hypothesis that curcumin may reduce systemic inflammation has relevance outside the realm of arthritis, since systemic inflammation has been linked to a wide variety of illnesses that manifest themselves in a variety of organ systems. One of these conditions is known as metabolic syndrome (MetS), and it is characterised by a number of risk factors, including insulin resistance,

hyperglycemia, hypertension, low high-density lipoprotein cholesterol (HDL-C), elevated low-density lipoprotein cholesterol (LDL-C), elevated triglyceride levels, and obesity, particularly visceral obesity. It has been shown that curcumin may alleviate a number of the symptoms associated with metabolic syndrome, including improved insulin sensitivity, suppression of adipogenesis, and a reduction in high blood pressure, inflammation, and oxidative stress. In addition, there is evidence that curcuminoids modulate the expression of genes and the activity of enzymes involved in lipoprotein metabolism, which results in a reduction in plasma triglycerides and cholesterol and an elevation in HDL-C concentrations [53]. This is the case because curcuminoids are responsible for the lipoprotein metabolism. It is known that pro-inflammatory cytokines are generated, despite the fact that the specific processes that cause this inflammation are not entirely understood, which links obesity and overweight to persistent low-grade inflammation. Researchers believe that cytokines like these are at the root of the difficulties that are connected with diabetes and cardiovascular disease. Taking steps to reduce inflammation is necessary for this reason. In a randomised, double-blind, placebo-controlled trial with a parallel-group design, 117 subjects with MetS were given either 1 gramme of curcumin plus 10 milligrammes of piperine to increase absorption or a placebo plus 10 milligrammes of piperine for a period of eight weeks. The trial was designed with a parallel-group format. Following supplementation with curcumin, there was a substantial drop in blood concentrations of tumour necrosis factor alpha (TNF-a), interleukin 6 (IL-6), transforming growth factor beta (TGF-b), and monocyte chemoattractant protein-1 (MCP-1) (p 0.001), as determined by within-group analysis. The blood levels of TGF-b were found to have reduced (p = 0.003) in the placebo group, whereas levels of IL-6 (p = 0.735), TNF-a (p = 0.138), and MCP-1 (p = 0.832) were not found to have changed. In a comparison between the curcumin group and the placebo group, it was shown that the curcumin group saw considerably larger decreases in blood concentrations of TNF-a, IL-6, TGF-b, and MCP-1 (p 0.001). Changes in other parameters remained statistically significant after adjustment for potential confounders, including changes in serum lipids and glucose levels, as well as the baseline serum concentration of the cytokines. The only parameter whose changes did not remain statistically significant was the concentration of IL-6. According to the findings of this research, taking curcumin supplements resulted in a

significant reduction in the blood concentrations of pro-inflammatory cytokines in participants who had MetS [11]. Curcuminoids were shown to be more efficient than the placebo in the reduction of serum LDL-C, non-HDL-C, total cholesterol, triglycerides, and lipoprotein a (Lp(a)), in addition to boosting HDL-C concentrations. This aspect of cholesterol reduction was also investigated in the research. On the other hand, it was discovered that the differences in the levels of serum LDL-C that occurred between the research groups were not significant. After making adjustments for the levels of lipids and body mass index that were present at the beginning of the study, the effects of curcuminoids on triglycerides, non-HDL-C, total cholesterol, and Lp(a) remained statistically significant. In the same research, the authors also observed indicators of oxidative stress. [Citation needed] In comparison to the group that received the placebo, the group that received the curcumin with piperine experienced a statistically significant increase in serum SOD activities (p 0.001), a reduction in MDA concentrations (p 0.001), and a reduction in C-reactive protein (CRP) concentrations (p 0.001) A secondary objective of their study was to do a meta-analysis of the data obtained from all of the randomised controlled trials so that they could determine the magnitude of the impact that curcuminoids had on plasma CRP concentrations. The quantitative data synthesis showed that curcuminoids had a much greater impact than the placebo in lowering the level of circulating CRP. The researchers came to the conclusion that a brief course of supplementation with a combination of curcuminoid and piperine dramatically improved both the oxidative and inflammatory states of individuals diagnosed with MetS. Therefore, curcuminoids might be considered to be natural CRP-lowering medicines that are both risk-free and very effective.

Side Effects:

The safety of curcumin has been well-documented for a very long time. For instance, the Allowable Daily Intake (ADI) value of curcumin is 0–3 mg/kg body weight, as stated in publications by JECFA (The Joint United Nations and World Health Organization Expert Committee on Food Additives) and EFSA (European Food Safety Authority). Curcumin has been shown to be both safe and effective in a number of clinical tests conducted on healthy participants. In spite of the fact that its safety has been shown beyond a reasonable doubt, certain unfavourable side effects have been documented. In a dosage response trial that

lasted for 72 hours, seven participants who received between 500 and 12,000 mg were seen to have diarrhoea, headaches, rashes, and faeces that was yellow [19]. In a different trial, some of the participants who took curcumin at doses ranging from 0.45 to 3.6 g per day for a period of one to four months reported experiencing nausea and diarrhoea, in addition to a rise in the levels of blood alkaline phosphatase and lactate dehydrogenase.

Conclusion:

Curcumin has garnered interest all around the globe because to the various health advantages it provides. These benefits seem to be largely exerted via the anti-oxidant and anti-inflammatory mechanisms that it has. It is possible to obtain these effects more effectively by combining curcumin with other substances, such as piperine, that considerably boost the compound's bioavailability. According to research, curcumin may be helpful in the treatment of illnesses involving oxidative stress and inflammation, as well as metabolic syndrome, arthritis, anxiety, and hyperlipidemia. It is also possible that it may aid in the control of inflammation and muscular soreness that are caused by exercise, hence improving recovery and future performance in persons who are active. In addition, even persons who have not been diagnosed with any health concerns may get some advantages from taking a relatively modest quantity of the substance.

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