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A Systemic Review of Curcumin's Clinical Effects in Boosting Cancer Therapy

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ABSTRACT

Curcumin, a natural substance, has shown to have anti-neoplastic activities in experimental animals and human studies. Angiogenesis, carcinogenesis, and tumor growth are all things that curcumin can curb. The therapeutic effects of curcumin in various types of tumors are investigated in this study using a organized assessment methodology. The effects of curcumin in the treatment of cancer are thoroughly evaluated using a systematic review technique. The study findings used in this report were culled from works that were made available in various online databases. These databases were thoroughly searched in accordance with the study's aims, and the significant publications were selected using the likely keywords "prevalence," "curcumin," "clinical characteristics," and "cancer." Clinical studies show curcumin enhances anti-metastatic protein expression, reduces side effects, extends chemotherapy and radiotherapy effectiveness, and prolongs patient survival when combined with chemotherapy drugs. The extensive review presented in this research shows that curcumin improves patients' quality of life by reducing the side effects of chemotherapy or radiation. Curcumin has been found in several trials to increase patient longevity and decrease tumour marker levels.

Keywords: Incidence, Turmeric extract, Manifestation, Neoplasm, Meta-analysis

INTRODUCTION

Our knowledge about molecular genetic causes of tumors has considerably improved during the past 25 years of research. It is now widely accepted that a series of molecular genetic alterations in cancer culminate in the loss of cellular differentiation and growth regulation, causing unregulated cell proliferation that eventually forms tumors [1]. The majority of cancer cases are found in developing nations, particularly those in Asia and South America. These nations have populations that are low- or middle-income by almost three-quarters. Typically, patients in underdeveloped countries have a one-third worse chance of surviving cancer than those in developed nations. [2].

Each year, around 90 lakhs new instances of cancer happen, with 40 lakhs occurring in wealthy nations and 50 lakhs in underdeveloped ones [3]. Cancer will rank among the world's top causes of sickness in the next decades, with 15 million new instances of different cancers anticipated by 2020. In addition, by 2030, cancer is anticipated to overtake all other causes of mortality [4]. Finding efficient and financially feasible therapies for patients in lowandmedium income nations is vital given the rising cancer statistics and the high cost of cancer treatments. The use of efficient and reasonably priced cancer therapies is what inspired this investigation.

Flavonoids being a significant subset of the same family of naturally occurring polyphenolic chemicals are produced as a byproduct of plant’s secondary metabolites and are used as medicinal herbs [5]. Recent studies have demonstrated the great effectiveness of flavonoids in the prevention and management of various illnesses, including cancer [6], cardiovascular disease [7], Alzheimer's disease [8], diabetes,

stroke, rheumatoid arthritis, and osteoporosis. Furthermore, there is solid proof that flavonoids have antiviral [9], anti-inflammatory [10], and antiallergenic properties [11].

In past few years, several studies were conducted on the extraction of herbal components, their characteristics in the treatment of various diseases (such as malignancies), and the specific processes by which these compounds work as drugs [12]. One of the many medicinal plants is curcumin, which has the chemical names "diferuloylmethane" and "longa Curcuma" with the chemical formula C21 H20 O6 [13]. The turmeric plant contains a powerful substance called curcumin.

It is found that curcumin, which accounts for 2 to 8% of turmeric compounds, is what gives turmeric its characteristic yellow or golden colour and is also responsible for many of its beneficial effects [14, 15]. Curcumin, however, possesses a low level of intrinsic toxicity as well as a number of unique qualities that have a significant influence on and uses in a variety of pharmacological advancements, including anti-inflammatory, antioxidant, antibacterial, and anti-tumor medications [16–18].

This study utilized a systematic review technique to provide the latest clinical research on curcumin's effects on cancer cell survival and metastasis, addressing the increasing cancer rates and high costs of treatments.

METHODS

To carry out this research, a comprehensive review methodology was used, and relevant studies' discoveries were extracted from articles published in international and nationaldatabases like, Web of Science (ISI), ScienceDirect, Google Scholar, PubMed, Scopus, and SID. The relevant publication records that met the study's objective were selected after a thorough search of these databases using the likely keywords "prevalence," "curcumin," "clinical characteristics," and "cancer." There were various processes involved in the process of selecting pertinent papers for the methodicalanalysis as well as the yield quality control procedure. First, depending on the search terms specified, all relevant articles were gathered.

Article evaluation standards

Original research papers, clinical trial studies, publications whose complete script and information are available, and revisions that studied the therapeutic effects of curcumin in diverse types of malignancies were the criteria used to choose articles for the meta-analysis.

Criteria for Literature Exclusion

Studies employing secondary data, meta-analyses, allies, case-control studies, systematic reviews, the descriptive studies, studies without data and cross-sectional studies from a sample of cancer patients were all disregarded. The use of EndNote (version X7, for Windows, Thomson Reuters), a citation management application, will help to get rid of duplicate publications and a lot of publications that belong to the same population.

Quality evaluation

The CONSORT checklist's 22 criteria were used to assess the quality of the chosen publications. The most recent CONSORT statement was released in 2001. RCT reporting has been demonstrated to be more scientifically sound when using the CONSORT statement [19, 20]. Every publication was evaluated by two independent reviewers (MM, SHR) in a blind manner. Each response was graded as either yes (1 points) or no (0 points), and certain responses were deemed not appropriate according to the characteristics of research. Low-quality papers were assessed to be excluded from the research if they had a quality score of less than 12. The highest possible quality score of 22 was thus used.

Curcumin’s effect on neovascularization, inflammation, and secondary spread in tumor cells

Angiogenesis involves a balance between antiangiogenic and angiogenic components, but in pathological situations like tumor formation, this control is compromised, causing tumor spread. The process of angiogenesis is influenced by several gene products that are made by various types of cells. Tumour

locations are typically where hypoxia occurs. Angiogenesis, the cell cycle, metastasis, and treatment resistance are all regulated and controlled by the protein recognized as hypoxia-inducible factor 1 (HIF-1) [21]. As was already noted, curcumin reduces the production of HIF1, a powerful promoter of angiogenesis.The main physiological input that triggers angiogenesis is hypoxia, which activates the transcription factor AP1. The transcription factor's expression is suppressed by curcumin [22]. It is well known that AP-1 and the Hypoxia-inducible factors, HIF-(1), are activated by hypoxic stress and beta-growth factor (TGF-) to increase VEGF production [23].

Curcumin has demonstrated inhibitory effects on the expression of membrane surface molecules implicated in cellular adhesion, including E-selectin, Intracellular Adhesion Molecule 1 (ICAM-1), and Vascular Cell Adhesion Molecule 1 (VCAM-1).[23]. Numerous cellular molecules that are involved in adhesion and the development and spread of tumours are impacted by curcumin [25]. ICAM-1, VCAM, and MMPs, which are critical for cellular adhesion and metastasis, were less expressed inside of cells as a result of curcumin treatment [26]. These molecules are involved in cellular adhesion and metastasis. Additionally, curcumin causes a rise in the expression of a number of anti-metastatic proteins, such as Ecadherin, NM23, a non-metastatic gene, and tissue inhibitor metalloproteinase (TIMP 2). The likelihood of metastasis would increase if E-cadherin were absent. E-cadherin is necessary to sustain cellular attachment, therefore [27]. Neoplasia and angiogenesis are related. The emergence of neovascularization, which is frequently a vital stage in the persistence and development of tumours, is referred to as "angiogenic" in this context. Numerous organs are protected from cancer by curcumin [21, 29-31, 32]. Many research have demonstrated curcumin's anti-inflammatory properties [22, 25, 28, 33]. It will be challenging to ascertain if curcumin's potent antioxidant activity also influences curcumin's capacity to decrease inflammation, though [22, 33]. As a strong anti-inflammatory agent, curcumin manifests its own effects in a variety of ways. First, curcumin prevents the NF- factor from being activated. [22, 25, 26, 33]. According to laboratory research, curcumin mitigates the oxidative stress brought on by tumors and restores NF-*kappa*B function. Since curcumin prevents the synthesis of TNF-, the amount of tumor-related T-cell apoptosis will be reduced [33].

Discussion

Curcumin's biological effects have recently been the subject of several studies. Curcumin has been found to have a variety of impacts in the treatment of cancer in more than 3000 research that have only lately been published. Curcumin has a number of beneficial qualities, including antioxidant, pro-apoptotic, anti-inflammatory, anti-fungal and, antiviral effects. Curcumin offers great potential as a therapy for cancer, AIDS, Alzheimer's, depression, diabetes, multiple sclerosis, psoriasis, intestinal inflammation, allergies, renal toxicity, and neurological illnesses [34-37]. The versatile chemical curcumin has a wide range of medicinal applications. Due to curcumin's ability to interact with many molecules and control several chemical pathways and their intended targets, it has a wide range of effects [38]. Natural substances target many biological and molecular features of cancer cells [39. Chemotherapy-resistant cells are made more susceptible to chemotherapy by curcumin, which turns around drug resistance mechanisms. Keyvani-Ghamsari et al.'s research has confirmed the tendency of curcumin as a chemical in neoplasia [40].

The results are rather inconsistent since there have been relatively few human clinical research. However, there are still a number of unresolved issues about dose, bioavailability, and the best indicators to check, and possible toxicity that required to be looked into in upcoming trials with sizable enough sample sizes [41]. Curcumin-containing nanocarriers improve curcumin's bioavailability, cell uptake, and anticancer effectiveness [42, 43]. Grell et al. treated 32 participants to dosages ranging from 100 to 300 mg per minute in another trial[44]. Howells et al. looked at 24 individuals with metastatic colorectal cancer who were older than 18 in 2019 using a histological diagnosis. The research suggests that curcumin can be used in conjunction with other medications to treat clinical symptoms, suppress and control malignancies, and prevent cancer development and metastasis.

CONCLUSION

The results of the trials that were included show that curcumin is an effective complementary therapy for cancer patients. Curcumin's pharmacological values are highlighted in this literature review by mining various databases. Curcumin demonstrates a variety of advantageous impacts in a number of different areas of cancer therapy, according to the investigation. It displays the capacity to make cancer cells more susceptible to traditional therapies like radiation and chemotherapy, hence increasing their effectiveness. Curcumin has also demonstrated promise in reducing tumour size, triggering apoptosis, and halting metastasis. These results imply that curcumin could have a major impact on cancer patients' clinical outcomes. Nevertheless, despite the encouraging findings, a number of limitations were found in the studies that were analysed. Small sample numbers, differences in curcumin formulations and doses, and a lack of standardised methodologies are some of these drawbacks. These elements influence the results' heterogeneity and necessitate more, well planned clinical studies to determine curcumin's ideal place in the treatment of cancer.This systematic review highlights curcumin's potential as a safe and effective adjunctive therapy in cancer treatment. Further research is needed to address limitations and establish consistent guidelines, but the evidence suggests it holds promise for improved cancer management strategies.

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