Handbook of Nutraceutical Volume I
Ingredients, Formulations, and Applications
Pathak Yashwant, Steven J. Schapiro

Curcumin: A Versatile Nutraceutical and an Inhibitor of Complement

Publication details
Kotwal Girish J
Published online on: 24 Nov 2009

Accessed on: 22 Nov 2023

PLEASE SCROLL DOWN FOR DOCUMENT

Full terms and conditions of use: https://www.routledgehandbooks.com/legal-notices/terms

This Document PDF may be used for research, teaching and private study purposes. Any substantial or systematic reproductions, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The publisher shall not be liable for an loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.
CHAPTER 13

Curcumin: A Versatile Nutraceutical and an Inhibitor of Complement

Girish J. Kotwal

CONTENTS

Introduction ............................................................................................................ 217
Distribution of Turmeric: The Current Source of All Curcumin ...................... 218
Preparation of Curcumin ................................................................................... 218
Activities of Curcumin ....................................................................................... 219
Problems with Curcumin and Human Trials ..................................................... 219
Future for Curcumin ............................................................................................ 220
Acknowledgements ............................................................................................. 220
References ............................................................................................................ 221

INTRODUCTION

Turmeric, a golden spice referred to as the Indian Gold, is prepared from underground rhizomes, of which the turmeric root (Curcuma longa) and the underground shoots form an interconnected underground, complex, finger-like structure. Turmeric belongs to the ginger family (Zingiberaceae) and for centuries has been considered in the Indian systems of medicine, such as Ayurveda and traditional Chinese medicine, to have therapeutic benefit. It is also a key ingredient of Indian, Malaysian, Chinese, Polynesian, and Thai curries, as well as western mustard preparations. In recent decades, the compound curcumin, a polyhydroxy phenolic compound that forms 4% of turmeric, has been found to have broad-spectrum antitumor activity [Sisodia et al. 2005], anti-neuroinflammatory activity [Kulkarni et al. 2005], and anti-Abeta plaque activity [Cole et al. 2004]. It is currently being marketed by several companies as a nutraceutical in treatment with possible
benefits in Alzheimer’s disease, arthritis, aging, a number of cancers, cardiovascular health, diabetes, obesity, and more. Some of the companies that made unsubstantiated claims about the commercial curcumin products have come under close scrutiny by the FDA. Therefore, curcumin products often indicate that they are natural health supplements that are not intended to diagnose, treat, cure, or prevent any disease. Dr. Bharat Aggarwal and his group at the M. D. Anderson Cancer Center in Houston, Texas, has worked and published extensively on the laboratory studies on the mechanism of action of curcumin [Aggarwal and Harikumar 2009]. They have demonstrated that curcumin mediates its effects by modulation of several important molecular targets, including transcription factors (e.g., NF-κB and epidermal growth factor-1), enzymes (e.g., COX2, 5-lipoxygenase, and iNOS), and cytokines (e.g., TNF, IL-1, IL-6, and chemokines) [Aggarwal and Harikumar 2009]. Recent studies have shown that curcumin is able to inhibit both pathways of complement activation [Kulkarni et al. 2005], and, because unregulated complement activity can cause serious autoimmune tissue damage in diseases such as rheumatoid arthritis, Alzheimer’s disease, macular degeneration, and atherosclerosis, curcumin has a potential for benefit in such conditions. Most of the polydroxy phenolic compounds of herbal origin are small-sized complement regulatory molecules that offer a great potential in the development of small-sized neuroprotective agents with an ability to cross the blood-brain barrier.

DISTRIBUTION OF TURMERIC: THE CURRENT SOURCE OF ALL CURCUMIN

Documented use of curcumin dates back to some several thousand years. Turmeric is grown in hot, moist climates and is cultivated and consumed in the Indian subcontinent; it is grown and prepared commercially in the southern Indian state of Kerala, as well as several other states in India. Turmeric is also grown in Africa, Australia, China, Indonesia, Peru, and the West Indies.

PREPARATION OF CURCUMIN

Curcumin can be extracted from the powdered turmeric by multiple ways such as a soap extraction process for producing water and oil-soluble curcumin [Stransky 1979], microwave-assisted extraction [Mandal et al. 2007], and others. The preferred extraction method would depend on the available facilities and the yield and purity required. Curcumin (from Sigma) used in our experiments was dissolved using minimum amount of ice-cold 0.1 M sodium hydroxide solution, and the final concentration was made to 2 mg/ml using ice-cold phosphate-buffered saline (0.154 M NaCl, pH 7.2). The solution was prepared in the dark, and the tubes used for holding the solution were covered with a metal foil to avoid photo degradation of curcumin.
ACTIVITIES OF CURCUMIN

Curcumin has several activities that influence, either alone or in concert, the health benefits of curcumin. It inhibits inflammation in several ways by inhibiting NF-κB-dependent gene transcription, by inhibiting COX2 and iNOS induction [Aggarwal and Harikumar 2009], and by inhibiting complement [Kulkarni et al. 2005]. The interaction of curcumin with the complement system has been studied extensively by our group and should serve as a model for other nutraceuticals interactions with human proteins and molecules. The complement system is made of 30 proteins, which when activated can form a cascade of events that can result in the destruction of bacteria, the neutralization of viruses, the recruitment of inflammatory cells, or the targeting of microorganisms for phagocytosis. The complement system is a powerful first line of defense against microorganisms, but, when unregulated or poorly regulated, it can cause destruction of the tissues and result in autoimmune damage. Our studies have revealed information regarding nature of binding of curcumin to the complement components as well as its mode of action on the complement pathway. To determine the interaction of curcumin with complement, Q-sense (D-300), a device based on quartz crystal microbalance with dissipation monitoring technology (QCMD), was used. In Q-sense, the change in frequency of a quartz-based sensor crystal resonating at its resonant frequency during adsorption of an adsorbing moiety is correlated with the change in mass of the adsorbed moiety. The energy dissipated during this adsorption is also recorded. The changes in frequency (f) and dissipation (D) are specific for a particular system comprising an adsorbing moiety and the ratio of change in dissipation to the change in frequency (dD/dF) gives information regarding the viscoelastic properties and adsorption kinetics of the system. QCMD is a well-established technique that offers advantages of real-time monitoring, speed, simplicity, sensitivity, and economy compared with the other routinely used techniques. It does not involve labeling of protein molecules, and therefore the chances of changes in conformation of the protein under optimal experimental conditions are less. Thus, it was decided to use Q-sense to study the interaction of curcumin with the complement components and compare with the vaccinia virus complement control protein, a well-characterized complement regulatory protein. Both curcumin and viral complement inhibitor from vaccinia virus (VCP) are known to inhibit the alternative and classical pathways of complement activation; hence, it was important to investigate their effect on the complement components C3 and C3b, which are central to both the pathways of complement activation. Our studies indicated that curcumin and VCP bound to both C3 and C3b with a greater affinity to C3 [A. P. Kulkarni and G. J. Kotwal, unpublished observation]. Some other activities of curcumin are as an antioxidant and inhibitor of apoptosis, tumor invasion, apoptosis, and an inducer of cell cycle arrest [Aggarwal and Harikumar 2009].

PROBLEMS WITH CURCUMIN AND HUMAN TRIALS

Several problems with curcumin usage need to be resolved before it becomes widely acceptable as an approved therapy with FDA-approved clinical trial-substantiated
claims. Curcumin has also quite often worked in laboratory studies but failed to show adequate therapeutic benefit in human trials [AIDS.org 2007]. Also, it is advisable that curcumin not be used in conjunction with chemotherapy, but very often that means that curcumin is recommended after chemotherapy has failed and precious time has been lost. The other problem is the high doses required to have a therapeutic effect as well as the problem with solubility and bioavailability [Higdon 2005]. It is 2,000-fold less active than VCP [Kulkarni et al. 2005b]. Because of the curcumin being metabolized in the body after being conjugated in the liver and intestine to form metabolites, such metabolites are possibly less active than the curcumin itself. Also, the absorption of curcumin happens mainly in the GI tract, making it less suitable for influencing organs outside the GI tract; therefore, there is a need to use some new delivery techniques, such as nanotechnology, to achieve better distribution to affected sites. Several investigators are attempting to better deliver curcumin by generating complexes of curcumin with various substances. One report uses the casein-micelle complexation to deliver curcumin as a drug nanocarrier to cancer cells [Sahu et al. 2008].

**FUTURE FOR CURCUMIN**

Curcumin is a nutraceutical that is extracted from turmeric. Because of considerable research in laboratories around the world, it has been postulated to have wide-ranging health benefits based on its activities studied. The characterization of its multiple interactions requires use of emerging technologies. An example of one such technology, QCMD, to characterize interactions of curcumin with the third component of the complement system has been mentioned above. The future of curcumin for the time being may be limited to its consumption as a part and parcel of turmeric added on a regular basis in generous amounts to food preparations, as has been done for centuries. Turmeric has stood the test of time and has a number of different additional applications in lotions and soaps. As more preclinical and clinical studies of pure curcumin are performed and the therapeutic benefit is evaluated in rigorous double-blind randomized trials, curcumin could find its potential promise in the laboratory getting realized. Its bioavailability and solubility issues will have to be resolved before a formulation of curcumin can replace the toxic chemotherapy that many cancer patients find difficult to tolerate.

**ACKNOWLEDGEMENTS**

The author thanks Dr. Amod Kulkarni for a useful discussion on the use of QCMD in studying the interactions of curcumin with complement components and for sharing unpublished data. Details of the work by Kulkarni et al. will be published in the Open Biochemistry Journal in 2010.
REFERENCES


