Review

Immunomodulatory effects of curcumin in allergy

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Recent years have witnessed a global increase in allergy and asthma, particularly in developed countries. Attempts to develop effective control measures for allergy and asthma resulted in the exploration of alternate medicines including herbal remedies traditionally used in old world countries. Turmeric is known for its multiple health restoring properties, and has been used in treating several diseases including several respiratory disorders. Turmeric is a common spice used in the culinary preparations in South and East Asian countries. The active component of turmeric is curcumin, a polyphenolic phytochemical, with anti-inflammatory, antiamyloid, antiseptic, antitumor, and antioxidative properties. Curcumin was reported to have antiallergic properties with inhibitory effect on histamine release from mast cells. The effectiveness of curcumin in allergy and asthma has been further investigated using a murine model of allergy. The results indicate a marked inhibition of allergic response in animals treated with curcumin suggesting a major role for curcumin in reducing the allergic response. The present review focuses on the results of research aimed to understand the immunomodulation induced by curcumin and its associated roles in the amelioration of allergy. These findings needed further evaluation, extrapolation, and confirmation before using curcumin for controlling allergy and asthma in humans.

Keywords: Allergy / Curcumin / Hypersensitivities / Immunomodulation / Turmeric

Received: July 28, 2007; revised: September 14, 2007; accepted: October 16, 2007

1 Introduction

The use of curcumin dates back to the time of Egyptian pharaohs and Indian culture more than 6000 years ago. The medicinal properties of turmeric have been known for millennia among ancient Indians and its medical properties have been written in the Ayurvedic texts where turmeric holds a high place as a body's cleanser, and today, modern science is finding a growing list of disease conditions where the active ingredient of turmeric has proven healing properties [1, 2].

Turmeric is a perennial plant cultivated throughout the tropics, especially in India, China, and Indonesia. It is used in a number of culinary preparations and curcumin gives the curry its unique flavor and color. Curcumin the major component of turmeric rhizome is gaining attention for its positive role in the treatment of a number of ailments. It is an effective antioxidant and has beneficial effects in inhibiting tumor growth. Its anti-inflammatory properties have been documented, so also its ability to retard some of the progression of acquire immune deficiency syndrome (AIDS). Turmeric was introduced into the pharmacopoeias as an indicator for testing the presence of alkalies. The yellow pigment in curcumin readily dissolves in alcohol to form a deep yellow solution, which turns to reddish-brown in alkalies. Curcumin is often added to food products as a coloring agent and to prevent oxidation-induced spoilage of food products. In addition to its culinary uses, curcumin has been used by traditional medicine for liver disease (particularly jaundice), indigestion, urinary tract diseases, blood purification, inflamed joints (rheumatoid arthritis), insect bites, dermatological disorders, and as a remedy in atherosclerosis [3].

The chemical structure of curcumin was determined in 1910, but it was only during the mid 1970s and 1980s, the

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Abbreviations: AIDS, acquired immune deficiency syndrome; **CAM,** complementary and alternative medicine; **CTL,** cytotoxic T lymphocyte; **NK,** natural killer; **NF-λB,** nuclear factor kappa B; **NO,** nitric oxide; **OVA,** ovalbumin

Figure 1. (A) The whole and (B) ground turmeric rhizomes.

potential uses of curcuminoids in medicine have been extensively studied. Curcumin is believed to have antioxidant, anti-inflammatory, and anticholesterolemic properties. Herbalists advise the use of turmeric to prevent heart disease and cancer, and to treat arthritis, and HIV infection. In Chinese traditional medicine, it is used to control hemorrhage, and to treat various diseases such as asthma and coryza. For centuries, turmeric has been used as a food additive, a medicinal agent, and a dye for cosmetics and fabrics. This record of safety has been one of the deciding factors that allowed the Food and Agricultural Organization and the World Health Organization expert committee on food additives to approve curcuminoids as natural food coloring agents [4, 5].

2 Allergy and complementary and alternative medicine (CAM)

The United States National Center for CAM (NCCAM), defines CAM as a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine (CAM basics. What CAM? Updated 2.2007; http://nccam.nih.gov/health/whatiscam/pdf/D347.pdf).

The historical importance of herbal medicine in the treatment of allergy and asthma is astounding, as most major Chinese traditional medicine, Ayurvedic medicine, and many ancient ethnical medicines used for the treatment of asthma are of plant origin. The different medical systems have shown different approaches to the control of diseases and afflictions. Inspite of the fact that modern medicine has transformed our understanding of diseases, particularly in the pathophysiology and innovative efforts in the successful control of a variety of diseases, a further need for an alternate option is much stronger today than before [6, 7]. One-third or more of all patients with asthma from UK and Australia resorted to herbal medicine [8].

Turmeric has been used in Asia particularly in ancient Indian medicine for allergy and asthma. In recent years, a number of studies have established the anti-inflammatory, antiseptic, antitumor, and antioxidant properties of curcumin. Since turmeric has been shown to have antiasthmatic properties we studied its effectiveness in allergy models developed in mice using either fungal allergen from *Aspergillus fumigatus* (results discussed below) or allergenic extract from *Hevea braziliensis* latex [9]. Our results indicate that curcumin downregulated Th2 response through decreased recruitment of eosinophils, reduced IgE antibody and cytokine production, and lesser inflammatory responses.

Table 1. Botanical classification of *C. longa*

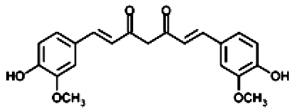
Kingdom	Plantae
Division	Magnoliophyta
Class	Liliopsida
Subclass	Zingiberidae
Order	Zingiberales
Family	Zingiberaceae
Genus	*Curcuma*
Species	*C. longa*

3 Biochemistry of turmeric

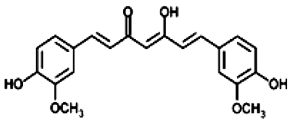
Curcuma longa (turmeric) is a member of zingiberaceae, the ginger family, distributed throughout tropical Africa, Asia, and the Americas (Table 1). This family of flowering plants that grows to a height of 3 – 5 feet consists of aromatic perennial herbs with horizontal rootstocks or tuberous rhizomes. The rhizome is the portion of the plant used medicinally; it is usually boiled, cleaned, and dried, yielding a yellow powder (Fig. 1). In the Ayurvedic medicine, turmeric is thought to have many medicinal properties and many in India use it as a readily available antiseptic and antibacterial agent. It is a popular dietary supplement in Asia and is a popular tea in the orient. Recent research has been focused on its antioxidant, hepatoprotective, anti-inflammatory, anticarcinogenic, and antimicrobial properties, in addition to its use in cardiovascular disease and gastrointestinal disorders [10]. The active constituents of turmeric are the flavenoid, curcumin, and volatile oils including tumerone, atlantone, and zingiberone. Other constituents include sugars, proteins, and resins (Table 2). The best researched active constituent is the polyphenol curcumin, which comprises 0.3 – 5.4% of raw turmeric. Curcumin, also known as natural yellow 3, is used as a food color and food additive (E100). It can exist as keto and enol forms and the former is predominant in solid phase while the enol form is more stable in solution state [11]. Pharmacologi-

Table 2. Chemistry of curcumin

Systematic name	(1*E*,6*E*)-1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione
Other names	Polyphenol curcumin; C. I. 75300; natural yellow 3
Molecular formula	$C_{21}H_{20}O_6$
Molar mass	368.38 g/mol
Appearance	Bright yellow to orange powder
Tautomeric forms	keto



enol



cally, curcumin has been found to be safe, has no significant toxicity reported. Clinical trials in humans indicated no dose-limited toxicity when administered at doses up to 10 g/day [12].

4 Antioxidant and anti-inflammatory properties of curcumin

Free radicals can originate from environmental chemicals causing tissue injury, infections, and initiate autoimmune processes. Antioxidants protect the body from damage from free radicals. An interesting benefit of turmeric and curcumin appears to be its significant antioxidant activity. Curcuminoids possess potential radical molecules that prevent free radical formation. Curcumin has been shown to be eight times more powerful than vitamin E in preventing lipid peroxidation and that curcuminoids are potent in neutralizing free radical molecules [13]. A recent study showed that the superoxide dismutase and catalase enzyme activities of curcumin prevent oxidative damage of Wistar rat lenses, preventing cataracts when cotreated with selenium [14]. It has been suggested that curcumin has role in reducing oxidative stress by downregulation of nitric oxide (NO) formation, scavenging or neutralizing free radicals, and by breaking the oxidative chain reaction caused by free radicals [15–17].

Inflammation results from a complex series of responses triggered by the immune system resulting in tissue damage. Inflammation is known to be associated with increased levels of lipid peroxides and free radicals, which are generated by inflamed tissues in the body. Moderate inflammation is necessary for the healing process, but continuous inflammation leads to chronic conditions like arthritis. Curcuminoids inhibit enzymes which participate in the synthesis of inflammatory molecules in the body. Curcumin's anti-inflammatory properties may be attributed to its ability to inhibit proinflammatory arachidonic acid, as well as neutrophil function during inflammatory process [18, 19], and is comparable in strength to steroidal and nonsteroidal drugs [18, 20, 21]. Turmeric triggers heat shock stress response resulting in the expression of Hsp27 and Hsp70, which stimulate the immune system. Since curcumin is a potent inhibitor of arachidonic acid metabolism, it is suggested that the mechanism of the stimulation by curcumin of the stress responses might be similar to that of salicylate, indomethacin, and nordihydroguaiaretic acid (NDGA) [22].

5 Effects of turmeric and curcumin in human disease

Animal studies involving rats and mice as well as *in vitro* studies utilizing human cell lines have demonstrated curcumin's ability to effectively inhibit carcinogenesis at three stages namely tumor promotion [23], angiogenesis [24, 25], and tumor growth [26]. Studies have suggested that curcumin has enormous potential in the prevention and therapy of cancer because of its ability to suppress proliferation of a wide variety of tumor cells [27, 28]. The anticarcinogenic effects of curcumin may be in part due to direct antioxidant and free radical scavenging effect or *via* suppression of several common mutagens and carcinogens [29–32]. Curcumin downregulate transcription factors including nuclear factor kappa B (NF-κB), Egr-1, and AP-1 [33], the expression of significant molecules such as COX2, LOX, NOS, MMP-9, uPA, tumor necrosis factor (TNF), chemokines, cell surface adhesion molecules, cyclin D1, and growth factor receptors such as EGFR and HER2. Curcumin has shown to inhibit the activity of protein tyrosine kinases, protein serine/threonine kinases, and c-Jun N-terminal kinase [34, 35]. Results of currently available data indicate that oral curcumin in patients with invasive malignancy or preinvasive lesions of the gastrointestinal tract has beneficial effects [36, 37].

Turmeric extract may benefit heart disease by decreasing cholesterol levels and other disease risk factors. Protective effect of curcumin against isoprenaline-induced myocardial ischemia in rat myocardium has been reported. This effect could be attributed to its antioxidant properties and inhibitory effects of xanthine dehydrogenase/xanthine oxidase conversion, and its resultant superoxide anion production [38]. Other studies have shown that animals supplemented with turmeric had lower total cholesterol levels than controls [39].

Constituents of *C. longa* exert several protective effects on the gastrointestinal tract [40, 41]. Sodium curcuminate, was found to inhibit intestinal spasm, and *p*-tolymethylcarbinol, a turmeric component, was found capable of increasing gastrin, secretin, bicarbonate, and pancreatic enzyme secretion [42]. Turmeric has also been shown in rats to

inhibit ulcer formation caused by stress, alcohol, indomethacin, pyloric ligation, and reserpine. This study demonstrated that turmeric extract significantly increased the gastric wall mucus in rats subjected to various gastrointestinal insults [43]. Ability of curcumin to inhibit *Helicobacter pylori*, cancer-provoking bacteria, associated with gastric and colon cancer has been reported [41].

Curcumin and its derivatives have been shown to inhibit Tat protein secreted by HIV1-infected cells that may encourage the pathogenesis of AIDS [44]. It has been reported that 18 HIV-positive patients who took curcumin daily for 20 wk had significant increase in CD4+ T cells counts compared to controls [45]. Curcumin has shown to inhibit the HIV-1 integrase protein and the anti-HIV activity of curcumin may be attributed to the inhibition of integrase [46].

Alzheimer's disease (AD) involves amyloid beta peptide (Abeta) accumulation, oxidative damage, and inflammation. Curcumin has shown potent antiamyloidogenic effects [47] and has role in the destabilization of preformed Abeta in the CNS, even though the mechanisms of the inhibition remains unclear. Curcumin has shown to reduce the accumulation of amyloid deposits and reduce the loss of proteins in the spaces between brain cells in mice [48]. By reducing the loss of protein in synapses, curcumin may also help to maintain memory.

6 Immunological effects of curcumin

In recent years considerable attention has been directed to understand the immunomodulatory effects of curcumin on the immune system. It has capabilities to modulate the activation of T cells, B cells, macrophages, neutrophils, natural killer (NK) cells, and dendritic cells, downregulate various proinflammatory cytokines and chemokines, and enhance antibody responses. The effect of curcumin on the development of T cell-mediated immunological responses largely remains unknown. Investigations directed to determine the effect of curcumin on mitogen/antigen-induced proliferation of splenic lymphocytes, induction of cytotoxic T lymphocytes (CTLs), lymphokine activated killer (LAK) cells, and the production of cytokines by T lymphocytes and macrophages have been carried out in recent years. The results showed that mitogen, IL-2, or alloantigen-induced proliferation of splenic lymphocytes, and development of CTLs is significantly suppressed at 12.5 – 30 μmol/L curcumin. The generation of LAK cells at similar concentrations was shown less sensitive to the suppressive effect of curcumin compared to the generation of antigen specific CTLs [49]. Curcumin irreversibly impaired these immune functions. Pretreatment (8 h) with curcumin to lymphoid cells failed to respond to the activation signals [49]. Curcumin also irreversibly inhibited the expression/production of IL-2 and IFNγ by splenic T lymphocytes and IL-12 and TNFα by peritoneal macrophages. Curcumin downregulated the activation of the transcription factor NF-κB without affecting the levels of constitutively expressed NF-κB. The latter result suggests that curcumin most likely retard cell proliferation, cell-mediated cytotoxicity (CMC), and cytokine production by inhibiting NF-κB target genes involved in the induction of these immune responses [49].

The effects of curcumin on mitogen (phytohemagglutinin, PHA) stimulated T-cell proliferation, NK cell cytotoxicity, production of cytokines by human peripheral blood mononuclear cells (PBMCs), and NO production in mouse macrophage cells, RAW-264.7 have been investigated. The results indicate that curcumin inhibits PHA-induced T-cell proliferation, IL-2 production, NO generation, and LPS-induced NF-κB but augments NK cell cytotoxicity. These results suggest that curcumin most likely inhibits cell proliferation and cytokine production by inhibiting NF-κB target genes involved in the induction of these immune parameters [50].

Recently it has been shown that curcumin inhibited IL-12 production in macrophages in a dose-dependent manner, leading to the inhibition of Th1 cytokine profile in CD4+ T cells, suggesting that a variety of known biological effects of curcumin also include anti-inflammatory activity. Thus curcumin may have significant implications also in the treatment of Th1-mediated immunological disorders [51].

The reported beneficial effects of curcumin in arthritis, allergy, asthma, atherosclerosis, heart disease, Alzheimer's disease, diabetes, and cancer might be in part due to its ability to modulate the immune system and hence its potential role as a therapeutic agent for immune disorders needed further attention [52].

7 Effect of curcumin in allergy

7.1 General

Recent years have witnessed a marked increase in allergy, particularly in developed countries, although a gradual and less dramatic increase also was noticed in developing nations. In line with the increase in prevalence, concerted efforts also have been directed to develop control measures. However, until now no strategies have been developed to investigate a long lasting cure for allergy and asthma, which still remains a chronic, life-long and incurable disease. Turmeric, containing curcumin has been used in Asian countries particularly in ancient Indian medicine for allergy and asthma treatment.

7.2 Animal models of allergy

Curcumin has been investigated in animal models of allergy to understand its role. It has been reported that curcumin is an effective antiallergic in type I and IV in animal models of allergy [53]. Curcumin has an inhibitory effect on histamine release from rat peritoneal mast cells [54].

The asthmatic property of curcumin has been recently investigated in a guinea pig model of airway hyperresponsiveness. The guinea pigs were sensitized with ovalbumin (OVA) to develop characteristic features of asthma, *e.g.*, allergen-induced airway constriction and airway hyperreactivity to histamine. Guinea pigs were treated with curcumin during sensitization to examine its preventive effect or after developing impaired airways features to study the therapeutic effects. Status of airway constriction and airway hyperreactivity were determined by measuring specific airway conductance. Curcumin treatment significantly inhibits OVA-induced airway constriction and airway hyperreactivity suggesting that curcumin is effective in improving the impaired airway features in the OVA-sensitized guinea pigs [55].

The antiallergic and antioxidative activities of curcumin and related compounds, such as glycosides, reductants and *bis*-demethoxy analogs, have currently been investigated by Suzuki *et al*. [56]. Their results suggest that the hydroxy groups of curcumin play a significant role in exerting both the antioxidative and antiallergic activities, and that most of the compounds develop the antiallergic activities through mechanisms related to both antioxidative and nonantioxidation activities [56].

7.2.1 Latex allergy model

We have tested curcumin in a murine model of latex allergy [9]. This model demonstrated an enhanced Th2 response represented by high serum IgE levels, peripheral blood and lung eosinophilia, Th2 cytokine expression, and lung pathology. Latex exposed animals when intragastrically (IG) treated with curcumin diminished the Th2 responses with a concurrent reduction in lung inflammation. Peripheral blood eosinophilia in curcumin-treated mice was significantly reduced, costimulatory molecule expression (CD80, CD86, and OX40L) on antigen presenting cells was decreased, and the expression of MMP-9, OAT, and TSLP genes was also attenuated [9]. Taken together these results indicate that curcumin downregulated Th2 response through reduced eosinophils, IgE antibody responses, cytokine, and inflammatory responses. This resulted in the overall reduction of allergic responses and therefore curcumin may have potential therapeutic value in controlling allergic responses resulting from exposure to allergens.

7.2.2 Curcumin in murine model of allergic aspergillosis

Recently our group studied the role of curcumin in an allergy model developed in mice using fungal allergen from *A. fumigatus* [57]. Mice were injected intraperitoneally (IP) with 100 μg of *Aspergillus* antigen in sterile PBS once every week for 2 wk. This was followed by intranasal (IN) inoculation of 50 μg of antigen in 30 μL of PBS. IN sensitization was done after lightly anesthetizing the animals with Halothane aerosol and the procedure was repeated every week for 13 wk. A group of mice was also treated with 200 μg of curcumin IG. Controls included both PBS treated mice (instead of *Aspergillus* antigen) and PBS and curcumin treated. The animal study was approved by the Veterans Affairs Animal Care and Use Committee.

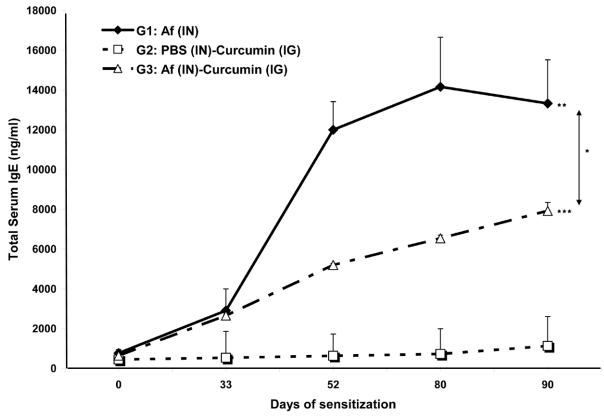


Figure 2. Total IgE responses (ng/mL) detected in *A. fumigatus* and curcumin treated mice. Data are presented as mean ± SEM, and *p*-values designated as $*p < 0.05$, $**p < 0.001$, and $***p < 0.0001$ *versus* the PBS controls.

Our results showed that total serum IgE demonstrated gradual increase from 2 wk after the exposure to *A. fumigatus* antigens until the end of the experiment. A significant suppression in the total IgE response ($p < 0.03$) was shown in mice treated with *A. fumigatus* and curcumin compared to *Aspergillus* antigen exposed mice. The normal controls treated similarly with curcumin showed no change in the total serum, [57] (Fig. 2).

Aspergillus specific IgG_1 showed significant increase in the serum of mice exposed to *Aspergillus* antigens. The specific antibody was detected 2–3 wk after the initial exposure and continued to remain high until the end of the experiment. There was *Aspergillus* specific IgG_1 detected in *A. fumigatus* and curcumin treated mice. IgG_{2a} antibody against *Aspergillus* showed only a slight increase in both groups of mice (data not shown). The eosinophils in *A. fumigatus* antigen treated mice continued to increase over the experimental period. This increase started to level off after 10–11 wk, similar to antibody levels. No demonstrable eosinophils were detected in the normal control mice treated with curcumin. However the *A. fumigatus* and curcumin treated mice showed only a slight increase and this difference between the groups were statistically significant (Fig. 3).

Antigen-induced spleen cell proliferation was studied using a mixture of recombinant *A. fumigatus* antigens, namely Asp f2, f3, and f4. There were no significant differences between the curcumin treated and untreated groups in the spleen cell stimulation (data not shown). Cytokine expression from spleen cells were studied by culturing the cells in complete RPMI medium in the presence of recombinant *A. fumigatus* antigen for 60 h. The superna-

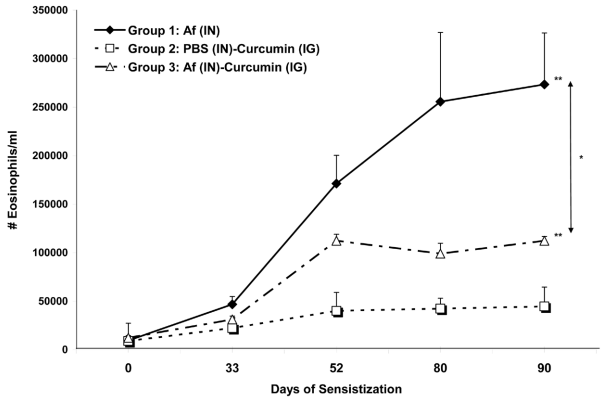


Figure 3. Peripheral blood eosinophils in mice sensitized with *A. fumigatus* and treated with curcumin. Data are presented as mean ± SEM, and *p*-values designated as $*p < 0.05$, $**p < 0.001$ *versus* the PBS controls.

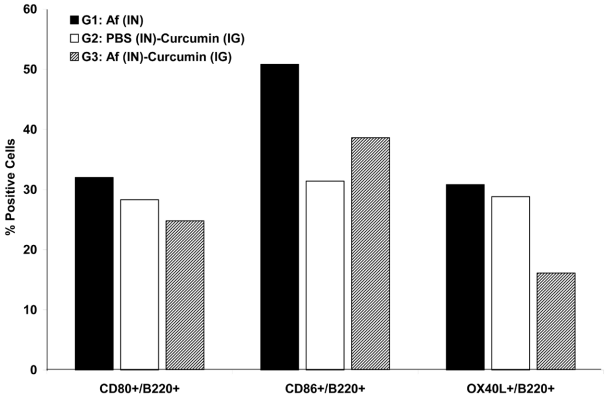


Figure 5. Expression of CD86, CD80, and OX40L costimulatory molecules on B220+ cells from the lungs of sensitized and nonsensitized mice. Lung cells were pooled from mice in each group and analyzed by flow cytometry.

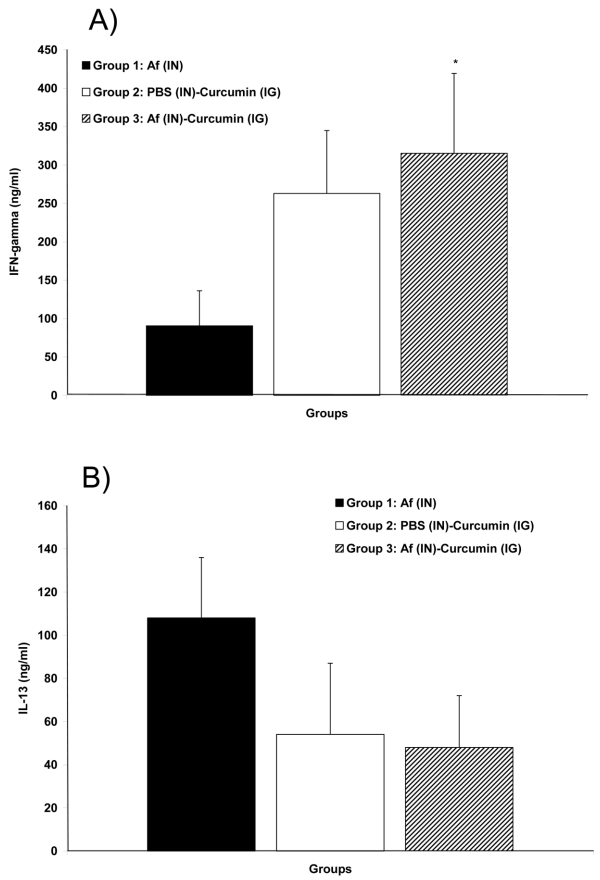


Figure 4. (A) IFNγ and (B) IL-13 levels in the supernatants of cultured spleen cells from mice sensitized with *A. fumigatus* antigens/treated with curcumin and controls. Data represent the mean ± SEM. **p*-values were considered to be significant.

tants were analyzed for IFNγ, IL-5, IL-4, IL-13, and IL-10 by ELISA. There was no IL-4 detected in any of the cultures, while significant amount of IFNγ was detected in spleen cells stimulated with *A. fumigatus* antigen from curcumin treated mice. However, mice challenged only with *A. fumigatus* showed no significant IFNγ production compared to control cultures without antigen (Fig. 4A). There was no difference in IL-5 levels in the culture supernatants of the *A. fumigatus* challenged and *A. fumigatus* and curcumin treated mice, although there was a trend toward lower level of IL-5 in the curcumin treated mice ($p < 0.16$). IL-10 levels in the culture supernatants of spleen cells from both groups failed to show any difference. The IL-13 levels, although not statistically different in the two groups, there was a trend toward lower IL-13 production in curcumin treated mice (Fig. 4B).

There was no major difference in the T cell or B cell numbers in the lungs. However, there was a reduction in the numbers of NK cell population in the *A. fumigatus*-curcumin treated mice compared to mice treat with *A. fumigatus* alone (data not shown). There was a reduction of CD80 and CD86 expression on B cells from the lungs of mice treated with *A. fumigatus* and curcumin compared to controls and *A. fumigatus* alone treated mice (Fig. 5). However, on macrophages, a reduction of CD86 expression was detected in *A. fumigatus* curcumin treated mice but not in the CD80 expression. It is interesting to note that OX40L expression was detected on the B cells of mice treated with curcumin, but not on the macrophages [57].

The histology of the lungs from the different groups of mice is shown in Fig. 6. Mice sensitized with *A. fumigatus* antigens showed significant interstitial inflammation with peribronchiolar and perivascular infiltrates. The inflammatory cells consisted primarily of small lymphocytes with plasma cells and epitheloid histiocytes. The histological examination showed broncho–alveolar epithelial hyperplasia, increased number of goblet cells, enhanced number of eosinophils, and occasional neutrophils. Minimal perivascular edema and moderate perivascular cuffing with infiltration of eosinophils, neutrophils, and mononuclear cells were also observed (Figs. 6C–F). The *A. fumigatus* sensi-

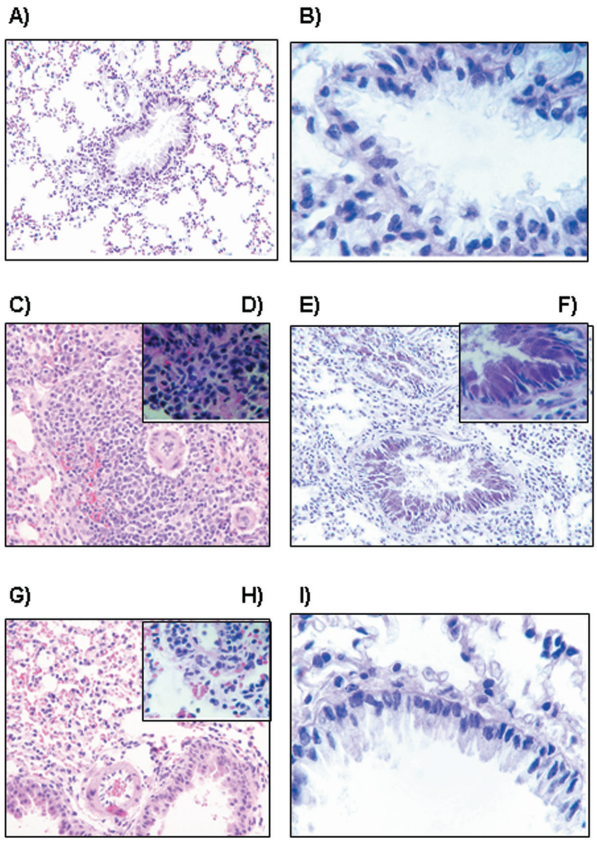


Figure 6. Histology of lungs from normal controls treated with PBS (A, B), *A. fumigatus* antigen sensitized mice, *A. fumigatus*/P, (C–F), and *A. fumigatus* antigen sensitized mice treated with curcumin, (G–I) *A. fumigatus*/cur. A, C, and G: H&E stain ×40; D and H inserts: H&E stain ×400; E: PAS stain ×40; B, F (insert) and I: PAS stain ×400.

tized mice treated with curcumin showed much fewer lesions and are consistently devoid of any eosinophils, although some mononuclear cells were still seen. There was less bronchial epithelial hyperplasia and very few goblets in this group of treated animals (Figs. 6G–I). Normal control mice and those treated with curcumin alone demonstrated no abnormality (Figs. 6A, B).

The *A. fumigatus* antigen-induced allergic model showed significant allergic response including total serum IgE, *Aspergillus* specific IgG_1, and eosinophils in peripheral blood and lungs. The inflammatory response in the lung, namely, perivascular, peribronchial, and alveolar responses are significantly evident in antigen exposed mice. However, mice exposed to *A. fumigatus* and treated with curcumin showed reduced response in all these features. IgG_{2a} response, though failed to show any difference among the two groups, IgG_{2b} showed an increase in curcumin treated mice [57].

There was marked difference in the tissue and peripheral blood eosinophils between the two groups, namely *A. fumigatus* exposed mice treated with and without curcumin. Similarly reduction in total serum IgE levels is an indicator of reduced Th2 response. Costimulatory molecules such as CD80, CD86, and OX40L, expression on B cells and macrophages showed reduced expression in curcumin and *A. fumigatus* treated mice compared to mice treated with *A. fumigatus* alone. These costimulatory molecules have major role in the expression Th2 cytokines and IgE responses. The overall immune response in curcumin treated mice showed a decrease may be due to the direct effect of curcumin on various factors of allergic responses. These results highlighted by the overall reduction of Th2 response and inflammation suggest the need for further studies [55]. In conclusion, curcumin treatment reduced the inflammatory responses in *A. fumigatus* exposed mice and consistently showed lower expression of Th2 cytokines and costimulatory molecules associated with allergenic responses [57].

Since no information is currently available on the effectiveness of curcumin to allergy caused by other allergens, it would be valuable to conduct such investigations in the future. This might result in elucidating the modulatory effects of curcumin in the Th2 response caused by different allergens such as pollens, dust mites, and indoor molds.

8 Conclusions

In addition of curcumin's popularity as a culinary spice, yellow dye, and preservative agent, it has been used as an antioxidant and anti-inflammatory agent with diverse healing beneficial effects. Today curcumin's established food and culinary demarcation are merging with the modern medicine and its cutting edge research and innovations. The research so far led us to consider the positive effectiveness of curcumin in the treatment and prevention of cancer, multiple sclerosis, arthritis, AIDS, and Alzheimer's disease. Curcumin has shown promise also in treating allergy related conditions although additional studies are needed to confirm its role and effectiveness.

We are thankful to Dr. Bryon D. Johnson and Dr. Jordan N. Fink for their interest and cooperation in the research.

The authors have declared no conflict of interest.

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