

## Food and Nutrition Report

# Aqueous Extract from Turmeric (*Curcuma Longa*) Inhibits Adenosine Deaminase Activity Significantly in Cancerous and Non Cancerous Human Gastric and Colon Tissues

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### Abstract

**Background:** We aimed to investigate possible effects of aqueous *curcuma longa* extract on adenosine deaminase (ADA) activity in cancerous and noncancerous human gastric and colon tissues in order to obtain information about anti cancer mechanism of *curcuma longa*.

**Methods:** Cancerous and noncancerous human gastric and colon tissues were used in the studies. The extracts were prepared in distilled water. Before and after treatment with the extracts, ADA activities in the tissue homogenates were measured.

**Results:** ADA activity was found to be higher in gastric tissue compared with colon tissue, but no differences were found between ADA activities of cancerous and noncancerous tissues. In the plant extract studies, it was found that curcuma extract significantly inhibited ADA activity both in cancerous and noncancerous gastric and colon tissues.

**Conclusion:** Our results suggest that aqueous extract from *curcuma longa* inhibits ADA activities in both gastric and colon tissues significantly. It is suggested that in addition to other proposed mechanisms, accumulated adenosine due to the inhibition of ADA enzyme might also play part in the anticancer properties of *curcuma longa*.

**Keywords:** Gastric cancer; Colon cancer; *Curcuma longa*; Adenosine deaminase.

### Introduction

Cancer is known as one of the major health problems for all people in the world. In addition to classical anticancer therapies, medicinal plants have a long history in the treatment of cancer [1] and studies related to anticancer agents from plant sources started about 60 years ago with the discovery and development of some alkaloids like vinca major and podophyllotoxins [2,3].

The rhizome of tumeric (*Curcuma longa*) as one of the medicinal

plants has been used for centuries in traditional folk medicine to treat cancer as it is known to have cancer preventive or therapeutic capacity [4]. The extracts from this plant have been shown to suppress multiple signaling pathways and inhibit cell proliferation, invasion, metastasis, and angiogenesis [5-7]. In addition to its relative safety, its multiple targeting potential makes it one of ideal agents for cancer researchers in order to investigate its preventive and treating potentials [8,9]. However, despite the important progress, there is still great lack to be replenished in the information on the anticancer mechanism of turmeric. *Curcuma longa* is known to have several components that may contribute to the observed beneficial effects besides the main active component, curcumin (diferuloylmethane). Moreover, possible roles of the structural gradients are not yet elucidated in detail. In fact, curcumin alone is found to be less effective than the combined in suppressing NFκB activation [10]. This means that some other constituents in *Curcuma longa* are also considerable for the total biological activity.

Adenosine deaminase (ADA) catalyses conversion reaction of adenosine to inosine. It is necessary for the human immune system [11] although its full function is not clarified yet [12]. ADA is proposed to play part in some physiological events like epithelial cell differentiation, neurotransmission, and gestation maintenance in addition to purine nucleotide breakdown and stimulation of release of some amino acids having excitatory function. It is also suggested for the coupling of A1 adenosine receptors and heterotrimeric G proteins [11-14].

Although some mechanisms are supposed for the action of *curcuma longa* in the cancer process, it is obvious that in addition to known mechanisms, there should be some others which are not known in detail yet. Therefore, we think that further studies are needed. As to the subject, it has been thought that investigation of the effects of aqueous extract from *curcuma longa* on the ADA activity in cancerous and noncancerous human tissues might give

useful results since ADA is a key enzyme in purine nucleotide metabolism, by this means in cancer process.

## Materials and methods

The study protocol was approved by the Ethical Committee of Clinical Research in Ankara University Faculty of Medicine, Ankara, Turkey. Sixteen cancerous gastric tissues and 16 noncancerous adjacent gastric tissues were obtained from patients with gastric cancer by surgical operation. Nine cancerous and 9 noncancerous colon tissues were similarly obtained from patients with colon cancer. Tissues were cleaned by saline solution and stored at  $-80^{\circ}\text{C}$  until analysis. In the analysis process, they were first homogenized (20%, weight/volume (w/v) in saline solution. After homogenization, homogenates were centrifuged at 5000 rpm for 30 min to remove debris and to obtain clear supernatant fraction. Analyses were performed in this fraction [15].

For the preparation of the extract, *curcuma longa* powder was soaked into the distilled water at the concentration of 10%, w/v and waited for 24 h at room temperature by rotating continuously. After the debris was removed, plant supernatants were centrifuged at 10000 rpm for 20 min and upper clear part was taken to be used in the assays.

Protein concentrations of the tissues were measured by the Lowry method [16] and ADA activity by the method of Guisti [17].

Statistical evaluations were made by Wilcoxon signed – rank test and *P* values lower than 0.05 were evaluated as significant.

## Results

Results were shown in Table 1. As seen from the table, *curcuma longa* extract significantly inhibits ADA activity both in cancerous and noncancerous gastric and colon tissues. Additionally, ADA activity was found to be higher in gastric tissue compared with colon tissue. There were however no differences between ADA activities of cancerous and noncancerous tissues as well.

**Table 1:** Mean  $\pm$  SD values for ADA activities (IU/mg protein) in the groups with and without *curcuma longa* extract.

Tissue	ADA activity without extract	ADA activity with extract
Colon, benign (n=9)	40.0 $\pm$ 21.8	16.4 $\pm$ 7.4*
Colon, malign (n=9)	49.2 $\pm$ 30.1	21.8 $\pm$ 16.5*
Gastric, benign (n=16)	102.9 $\pm$ 77.8	42.0 $\pm$ 26.6*
Gastric, malign (n=16)	98.0 $\pm$ 89.8	46.0 $\pm$ 44.8*

\*  $P < 0.05$  Values in the groups with and without extract was compared statistically by the Wilcoxon signed – rank test.

## Discussion

Plants are the important sources of effective conventional drugs for the treatment of some types of cancers, leading to the development of potential novel agents [18,19].

Of them, *curcuma longa* is reported to be useful for some common ailments. In addition to antimicrobial, antiinflammatory and antioxidant activities, it has been found to possess chemopreventive activity for a wide variety of cancers [8,9,20-23]. In a recent study, it has been reported that its components show antiproliferative activities [10]. The major active constituent

present in turmeric is curcumin (or diferuloylmethane), which is linked with the suppression of mutagenesis, inhibition of nuclear factor- $\kappa$ B (NF- $\kappa$ B) activation, suppression of cyclin D1, induction of cytochrome C release, activation of caspases and with anti-angiogenic effects through downregulation of vascular endothelial growth factor [24-28]. Curcumin has been used in clinical trials for some time for the treatment of various cancers [29,30]. In a study, it has been found that *curcuma longa* extract shows significant inhibitory effect on the colony-forming ability of the highly metastatic PC-3M prostate cancer cell line [31]. Further studies showed that only a fraction possessed this inhibitory effect in clonogenic assays (31ref.). Despite the progress, the molecular targets and mechanisms of action of *curcuma longa* are not identified fully as yet. Therefore, it seems valuable to investigate its effects on some critical components having functionality in the living cells in the body.

In this regard, ADA seems of importance since it is a key enzyme in the purine metabolism, inhibition of which may give selective advantage to combat with cancer. Therefore, investigation of possible effects of some plants including *curcuma longa* may give some useful information about their anticancer potential mechanisms. From a scientific perspective, the use of ADA inhibitors has helped enormously in understanding the mechanism of action of adenosine metabolites and analogs whose catabolism was previously neglected with respect to their specificities of action. ADA inhibitors have also enabled us to understand the regulatory processes associated with immunodeficiencies characterized by a lack of ADA, and to further understand the maturation of the immune response [32]. Of them, pentostatin is a nucleoside analog that inhibits the activity of the adenosine deaminase enzyme. Inhibition of adenosine deaminase blocks the deamination of adenosine to inosine and deoxyadenosine to deoxyinosine in the purine salvage pathway. The accumulation of metabolites inhibits ribonucleotide reductase, which depletes the nucleotide pool and limits DNA synthesis [33].

Looking at our results, it seems that ADA activity is higher in gastric tissue compared with colon tissue, but there are no differences between ADA activities of cancerous and noncancerous cancer tissues for both tissues. Our results however suggest that components of aqueous extract from *curcuma longa* inhibit ADA activities in both gastric and colon tissues significantly. Inhibition degrees in ADA activity are almost the same in the cancerous (malign) and non cancerous adjacent tissues (benign).

In conclusion, it seems quite possible that in addition to other proposed mechanisms, accumulated adenosine due to the inhibition of ADA enzyme might also play an important part in the anticancer properties of *curcuma longa*.

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