Curcumin

Plant extract therapy has been the cornerstone of cancer treatment for many years. The natural component curcumin demonstrated antineoplastic effects on different type of tumor cells.

Curcumin (Cur), is a natural polyphenol of Curcuma longa.

Due to its poor aqueous solubility and low biological availability, the clinical application of Cur is quite limited.

It is the principal curcuminoid of turmeric, which is a member of the ginger family (Zingiberaceae). Turmeric's other two curcuminoids are desmethoxycurcumin and bis-desmethoxycurcumin.

Curcumin can exist in several tautomeric forms, including a 1,3-diketo form and two equivalent enol forms. The enol form is more energetically stable in the solid phase and in solution.

Curcumin has a bright-yellow color and may be used as a food coloring. As a food additive, its E number is E100.

see Curcumin for Traumatic Brain Injury.

In a study Yin et al., found that expression of miR 326, a tumor suppressor microRNA in various tumor types, resulted in a marked increase of curcumin-induced cytotoxicity and apoptosis and a decrease of proliferation and migration in glioma cells. Moreover, they found that combination treatment of miR-326 and curcumin caused significant inhibition of the SHH/GLI1 pathway in glioma cells compared with either treatment alone, independent of p53 status. Furthermore, in vivo, the curcumin-induced increase in miR-326 expression altered the anti-glioma mechanism of this combination treatment, which further reduced tumor volume and prolonged the survival period compared to either treatment alone. Taken together, this data strongly support an important role for miR-326 in enhancing the chemosensitivity of glioma cells to curcumin [1].

Results suggest that curcumin not only protects astrocytes from H2O2-induced oxidative stress but also reverses the mitochondrial damage and dysfunction induced by oxidative stress. A study also provides evidence for protective role of curcumin on astrocytes by showing its effects on attenuating reactive astrogliosis and inhibiting apoptosis [2].

A study found that CUR may be effective in nervous system problems induced by neurotoxic agents. However, due to the lack of information on human, more investigations are needed to determine the efficacy of CUR as an antidote matter [3].

Results of investigations proved that curcumin is a natural compound potentially useful in the fight against glioblastoma (GB) [4].

Mukherjee et al., used the non-invasive strategy of intranasal (IN) delivery of a glioblastoma-directed adduct of curcumin (CC), CC-CD68Ab, into the brain of mouse GBM GL261-implanted mice to study the effect of CC on tumor remission and on the phenotype of the tumor-associated microglial cells (TAMs). The treatment caused tumor remission in 50% of GL261-implanted GBM mice. A similar

rescue rate was also achieved through intraperitoneal infusion of a lipid-encapsulated formulation of CC, Curcumin Phytosome, into the GL261-implanted GBM mice. Most strikingly, both forms of CC elicited a dramatic change in the tumor-associated Iba1+ TAMs, suppressing the tumor-promoting Arginase1high , iNOSlow M2-type TAM population while inducing the Arginase1low , iNOShigh M1-type tumoricidal microglia. Concomitantly, we observed a marked induction and activation of microglial NF-kB and STAT1, which are known to function in coordination to cause induction of iNOS. Therefore, our novel findings indicate that appropriately delivered CC can directly kill GBM cells and also repolarize the TAMs to the tumoricidal M1 state [5)].

Nanomicelles loaded with Cur were formulated by a self-assembly method with biodegradable monomethoxy poly(ethylene glycol)-poly(lactide) copolymers (MPEG-PLAs). After encapsulation, the cellular uptake was increased and Cur could be released from MPEG-PLA micelles in a sustained manner. The Cur-loaded MPEG-PLA micelles (Cur/MPEG-PLA micelles) exhibited an enhanced toxicity on C6 and U251 glioma cells and induced more apoptosis on C6 glioma cells compared with free Cur. Moreover, the therapy efficiency of Cur/MPEG-PLA micelles was evaluated at length on a nude mouse model bearing glioma. The Cur/MPEG-PLA micelles were more effective on suppressing tumor growth compared with free Cur, which indicated that Cur/MPEG-PLA micelles improved the antiglioma activity of Cur in vivo. The results of immunohistochemical and immunofluorescent analysis indicated that the induction of apoptosis, antiangiogenesis, and inhibition of cell proliferation may contribute to the improvement in antiglioma effects. Our data suggested that Cur/MPEG-PLA may have potential clinic applications in glioma therapy [6)].

Primary cortical neurons were cultured and were injured by ferrous chloride, z.vad.fmk was applied to block apoptosis, curcumin was administrated to protect neurons, necrostatin-1 was applied to inhibit necroptosis if needed. Cell viability was measured by detecting lactate dehydrogenase activity in lysates of surviving cells, and assessed by cell counting kit-8. The expression of receptor interacting protein 1 was detected by immunoblot and immunofluorescence. Results showed that necroptosis mainly occurred in the concentrations of ferrous chloride ranging from 100 to 200μM, curcumin attenuated necroptosis in a dose-dependent manner. Furthermore, curcumin decreased expression of receptor interacting protein 1 in a dose- and time-dependent manner. Taken together, these findings suggest that curcumin protects against iron induced neurotoxicity in primary cortical neurons by attenuating necroptosis [7)].

Case series

Thirteen glioblastoma patients ingested 70 mg micellar curcuminoids [57.4 mg curcumin, 11.2 mg demethoxycurcumin (DMC), and 1.4 mg bis-demethoxycurcumin (BDMC)] three times per day for 4 days (total amount of 689 mg curcumin, 134 mg DMC, and 17 mg BDMC) prior to planned resection of their respective brain tumors. Tumor and blood samples were taken during the surgery and analyzed for total curcuminoid concentrations. (31)P magnetic resonance spectroscopic imaging was performed before and after curcuminoid consumption.

Ten patients completed the study. The mean intratumoral concentration of curcumin was 56 pg/mg of tissue (range 9-151), and the mean serum concentration was 253 ng/ml (range 129-364). Inorganic phosphate was significantly increased within the tumor (P = 0.034). The mean ratio of phosphocreatine to inorganic phosphate decreased, and the mean intratumoral pH increased (P =

0.08) after curcuminoid intervention.

Oral treatment with micellar curcuminoids led to quantifiable concentrations of total curcuminoids in glioblastomas and may alter intratumoral energy metabolism [8].

1)
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