Letter to Editor

Synthetic curcumin: An update on efficacy and safety

Sir,

Curcumin, a dietary molecule extracted from the rhizome of curcuma longa (turmeric), is a widely known colorant (E100) used in supplements, food and beverages, and cosmeceuticals worldwide.[1] It is the principal component (about 77%) in the natural turmeric extract along with other chemical constituents, which are commonly known as "curcuminoids." Other chemical constituents are demethoxycurcumin (about 17%) and bisdemethoxycurcumin (about 3%). Turmeric contains curcumin, several of its derivatives, oils, resins and other co-factors from the rhizome; thus there is a possibility of contamination of natural curcumin with other substances. During the growth cycle of plant contamination from the environment, and from the extraction and purification processes such as fertilizers, heavy metals, spores, solvents, etc., is also common. Synthetic curcumin (S-curcumin) provides a solution and being a pure compound it eliminates unspecified impurities.[2] In last few years, S-curcumin was assessed in different biological studies and compared with natural curcumin/curcuminoids. Safety profile of S-curcumin was also established and discussed in this manuscript.

Scientists at University of Bern, Switzerland have compared synthetic and natural curcumin in oral mucositis. They have found that synthetic and natural, both curcumin were equivalent in a number of *in vitro* biological assays (bactericidal activity, ability to inhibit bacterial adherence and invasion to epithelial cells, and power to inhibit epithelial cytokine/chemokine release) mimicking aspects of bacteria-induced mucosal surface inflammation. The concentrations used in the studies were far below the daily allowances as a food additive for oral curcumin (E100), which amounted to 3 mg/kg/day of natural curcumin. S-curcumin used at a concentration of 200 μM (e.g. 10 ml of mouth rinse 4 times daily amounted to a total daily dose of 2.94 mg) was in the range declared safe by the European Food Safety Authority. They have concluded that S-curcumin is a safe and highly purified molecule, lacking the batch-to-batch variation of curcumin content, equipotent, odorless, tasteless and more palatable alternative to natural curcumin for the development of an oral anti-mucositis agent.[1]

A clinical trial with chemically manufactured curcumin (S-curcumin) at National Taiwan University Hospital and Kaohsiung Medical College, Taiwan demonstrated that curcumin was not toxic to humans up to 8000 mg/day when taken by mouth for 3 months. This was an important study to establish safety profile of chemically manufactured curcumin. The study was performed in a total of 25 patients (13 male and 12 female) having one of the following preinvasive malignant or high-risk premalignant conditions of urinary bladder cancer, arsenic Bowen's disease of the skin, uterine cervical intraepithelial neoplasm, oral leukoplakia, and intestinal metaplasia of the stomach. At the end of study, histologic improvement of precancerous lesions was noticed in 1 of 2 patients with presumed bladder carcinoma, 2 of 7 patients of oral leukoplakia, 1 of 6 patients of intestinal metaplasia of the stomach, 1 of 4 patients with cervical intraepithelial neoplasia and 2 of 6 patients with Bowen's disease.[3]

In vitro cytotoxic activities, relative nuclear factor κB (NF-κB) inhibition and effect on NF-κB-regulated gene products in human myeloid leukemic KBM-5 cells were reported almost similar with synthetic and natural curcumin.[4] The efficacy of S-curcumin was also validated for anti-oxidant, anti-inflammatory [tumor necrosis factor-alpha (TNF-α) induced NF-κB expression] activities and through comparative pharmacokinetics. S-curcumin has exhibited high anti-oxidant activity with total ORAC (oxygen radical absorbance capacity) value, over 1,500,000 μmole TE/g.[2] Antioxidant potential and free radical scavenging abilities of S-curcumin were evaluated using *in vitro* models such as, reducing potential, 1,1-diphenyl-2-picryl-hydrazil (DPPH), superoxide, hydrogen peroxide and nitric oxide radical scavenging; and the efficacy was reported in a dose-dependent manner. Results were reproduced in *ex vivo* models such as erythrocyte lipid peroxidation and erythrocyte hemolysis.[5] The anti-inflammatory activity was studied in human 293T cells. The level of NF-κB was found 49.33 μmol QE/g of quercetin activity when tested at 1 mg/ml of S-curcumin. This has indicated that S-curcumin down-regulated TNF-α induced NF-κB expression. The pharmacokinetic profile of synthetic and natural curcumin was also comparable in female Wistar rats. Interestingly, the emission of greenhouse gases measured by "carbon footprint analysis" indicated that the carbon footprint for the curcumin produced by chemical synthesis was lower than that of manufacturing of natural curcuminoids from its natural source.[2]

In another study, the anti-inflammatory and anti-allergic efficacy of S-curcumin was confirmed *in silico*, *in vitro* and *in vivo*. Primary *in silico* docking studies ascertained the multi-target potency of curcumin with crucial inflammatory mediators such as lipoxygenase, P38 mitogen-activated protein kinase, protein kinase C and extracellular signal-regulated kinase. The high safety profile of S-curcumin was observed from the acute toxicity study. The acute oral LD_{50} of S-curcumin was found to be >5000 mg/kg of body weight in female Sprague–Dawley rats.[6] Different synthetic analogues of curcumin also exhibited encouraging results in various studies.[4]

Synthetic curcumin offers consistent product quality and avoids problems associated with extracts of natural products such as uncontrolled outputs, variation in potency of extract due to variation in natural plant materials, co-occurring impurities, etc. High purity of S-curcumin ensures standardization of formulations with consistent activity and potency. Being manufactured synthetically, it also avoids exploitation of large quantities of turmeric that otherwise can be used as a food product in a sustainable manner.[2]

Roopesh Jain, Archana Tiwari

School of Biotechnology, Rajiv Gandhi Proudyogiki Vishwavidyalaya, Bhopal, Madhya Pradesh, India

Address for correspondence: Mr. Roopesh Jain, School of Biotechnology, Rajiv Gandhi Proudyogiki Vishwavidyalaya, Airport Bypass Road, Gandhinagar, Bhopal, Madhya Pradesh, India.
E-mail: science.roopesh@gmail.com

REFERENCES

1. Lüer SC, Goette J, Troller R, Aebi C. Synthetic versus natural curcumin: bioequivalence in an *in vitro* oral mucositis model. BMC Complement Altern Med 2014;14:53.
2. Jain R. Nature identical curcumin. Int J Appl Basic Med Res 2013;3:134.
3. Cheng AL, Hsu CH, Lin JK, Hsu MM, Ho YF, Shen TS, *et al.* Phase I clinical trial of curcumin, a chemopreventive agent, in patients with high-risk or pre-malignant lesions. Anticancer Res 2001;21:2895-900.
4. Ravindran J, Subbaraju GV, Ramani MV, Sung B, Aggarwal BB. Bisdemethylcurcumin and structurally related hispolon analogues of curcumin exhibit enhanced prooxidant, anti-proliferative and anti-inflammatory activities *in vitro*. Biochem Pharmacol 2010;79:1658-66.
5. Borra SK, Gurumurthy P, Mahendra J, Jayamathi KM, Cherian CN, Chand R. Antioxidant and free radical scavenging activity of curcumin determined by using different *in vitro* and *ex vivo* models. J Med Plants Res 2013;7:2680-90.
6. Venkata M, Sripathy R, Anjana D, Somashekara N, Krishnaraju A, Krishanu S, *et al. In silico*, *In vitro* and *In vivo* assessment of safety and anti-inflammatory activity of curcumin. Am J Infect Dis 2012;8:26-33.

Access this article online

Quick Response Code:

Website: www.advbiores.net

DOI: 10.4103/2277-9175.179860

How to cite this article: Jain R, Tiwari A. Synthetic curcumin: An update on efficacy and safety. Adv Biomed Res 2016;5:65.