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Anticancer activity of crocin against cervical carcinoma (HeLa cells): Bioassessment and toxicity evaluation of crocin in male albino rats

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ABSTRACT

The present study was aimed to investigate anticancer activity of crocin against cervical carcinoma and bioassessment and toxicological evaluation in male albino rats. Effect of crocin on cell viability (anticancer activity) was determined against cervical carcinoma cells. Chronic effect of crocin on body weight changes, serum enzymes, serum biochemical markers, lipid peroxidation, hematological markers and DNA damage in male albino rats were determined. Cell survival rate was reduced 98.4, 95.7, 87.2, 81.1 and 73.1% at 25, 50, 75, 100 and 125 mg/l of crocin respectively. Cell viability was reduced 97.1, 96.4, 85.5, 78.4 and 70.2% at 25, 50, 75, 100 and 125 mg/l of crocin respectively. Crocin reduced body weight significantly at 30 and 60th day. Alanine transaminase (ALT), aspartate transaminase (AST), lactate dehydrogenase (LDH), alkaline phosphatase (ALP), blood urea nitrogen (BUN), creatinine, bilirubin, albumin and total protein were decreased, while glucose, cholesterol, TG, and GSH were increased. Hemoglobin (Hb), white blood cells (WBC), lymphocytes, neutrophil and packed cell volume (PCV) were altered following crocin treatment. Necrosis, fibrosis, mononuclear infiltration, angiogenesis and DNA fragmentation were also noted. Taking all these data together, it is suggested that the crocin could be a potential antitumor agent against cervical carcinoma. However, the altered histological, biochemical and hematological markers may lead to an adverse effect on the cellular metabolism and physiological activity.

1. Introduction

Crocin is a di-gentiobiose ester and a water-soluble carotenoid of *C. sativa*. Carotenoids act as biological antioxidants and protect the cells from free radicals and singlet oxygen [1]. Crocin is a natural carotenoid compound and commonly in the flowers crocus and gardenia [2]. Crocin is a medication that is sold legally without a doctor's prescription and readily available to the patients. Crocin is used to treat muscular pain, cold, flu, tooth decay, headaches, and itches [2]. It is a safe drug at an average dose, but an overdose of crocin shows symptoms like nausea, vomiting, stomach upset, dizziness, constipation, restlessness, headaches, and collapse. Liver and kidney impairments occur due to an overdose of crocin [2, 3].

Crocin is known have several pharmacological effects such as the hypotensive effect [4], antidepressant activity [5] renoprotective [6], improve sexual activity [7], antioxidant [8], inhibition of lipid peroxidation in renal [9], hippocampal [10] and muscle skeletal homogenates in rats [11]. Crocin increases the blood flow in the choroid and retina and could be used in the treatment of ischemic-based retinopathy, and age-dependent macular degeneration. Moreover, crocin inhibits skin tumor growth [12], improves the learning behavior that has been impaired by ethanol [13] or hyoscine [14], and reduce the ethanol inhibitory effect in rats [15]. The LD50 values of saffron extracts of stigma and petal in mice. The aqueous stigma extracts decreased hematocrit level, hemoglobin (Hb) and erythrocytes content. However, it did not induce any pathological effects [16]. Saffron level between 1.2 and 2 g induced nausea, vomiting, diarrhea and bleeding [17]. Higher concentration of saffron induces hematological and biochemical changes in healthy adult volunteers [18].

The high oral and intraperitoneal doses of crocin did not cause death within two days experiment. Platelets and creatinine levels were reduced following crocin treatment. The weight loss and a reduction in food intake were found at this dose level. Reduced albumin and alkaline phosphatase (ALP) and increased low-density lipoprotein (LDL) level were also found. Reduced alveolar size in lungs was observed following crocin (180 mg/kg bwt) in rats [19]. The present study was aimed to investigate anticancer activity of crocin against cervical carcinoma and bio-assessment and toxicological evaluation in male albino rats.

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2. Materials and Methods

Crocin (Catalog No.17394), dimethyl sulphoxide (DMSO), sulforhodamine B (SRB), Dulbecco's Modified Eagle's Medium (DMEM), fetal bovine serum (FBS), penicillin–streptomycin, trypsin-EDTA, agarose, ketamine hydrochloride, xylazine, chloroform, 3-(4, 5-dimethylthiazolyl)-diphenyl tetrazolium bromide (MTT) and n-hexane were obtained from Sigma-Aldrich (Shanghai, Yangpu, China). Aspartate aminotransferase (AST), alanine aminotransferase (ALT), ALP, and lactate dehydrogenase (LDH) enzyme assay kits were obtained from Bio-Rad (Pudong, China).

2.1. Animals

Male albino Wistar strain rats (160–180 g) were purchased from the animal house of Zhuzhou Central Hospital. Animals were kept at room temperature with a relative humidity of 60 ± 5% and a photoperiod of 12 h/day in polypropylene cages. Animal experiments were approved by the ethics committee of Clinic laboratory of Zhuzhou Central Hospital. All the animals were treated according to internationally accepted ethical procedures.

2.2. Anticancer activity

2.2.1. Cell Culture

HeLa cells were obtained from the American Type Culture Collection (ATCC) (Manassas, VA 20110 USA). Cells were grown under standard growth medium containing 10% FBS and 1% penicillin–-streptomycin at standard conditions.

2.2.2. SRB assay

Cells were cultured and grown at a density of 1.5×10^4 cells/well into 96-well plates, and treated with crocin at different concentrations (25, 50, 75, 100 & 125 mg/l) for 72 h. Spectral data were collected under a 96 well plate reader at 510 nm to calculate the cell survival rate [20].

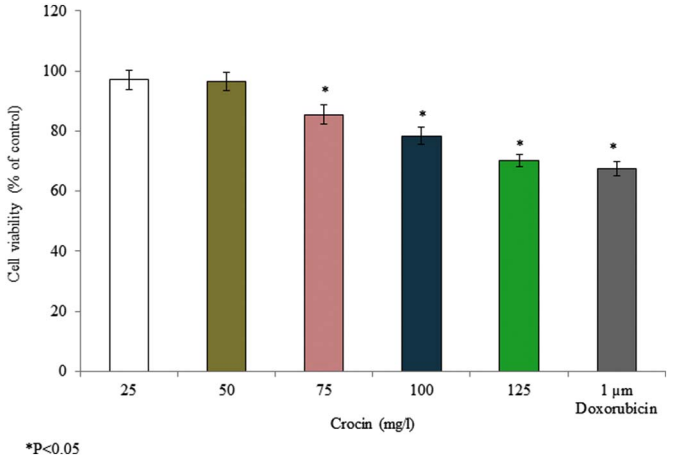

Fig. 2. Anticancer activity of crocin against human cervical carcinoma cells. Cell viability was calculated with reference to control and expressed as a percentage.

2.2.3. MTT assay

Cells were cultured and grown at a density of 1.5×10^4 cells/well into 96-well plates, and treated with crocin at different concentrations (25, 50, 75, 100 & 125 mg/l) for 72 h. Spectral data were collected under a 96 well plate reader at 570 nm to calculate the cell viability [21].

2.2.4. Experimental groups and treatment

Rats were grouped into 5 containing six rats each. Group I received normal saline (control), group II, III, IV, and V received crocin and served as treatment at 1, 15, 30 and 60 days respectively. Crocin

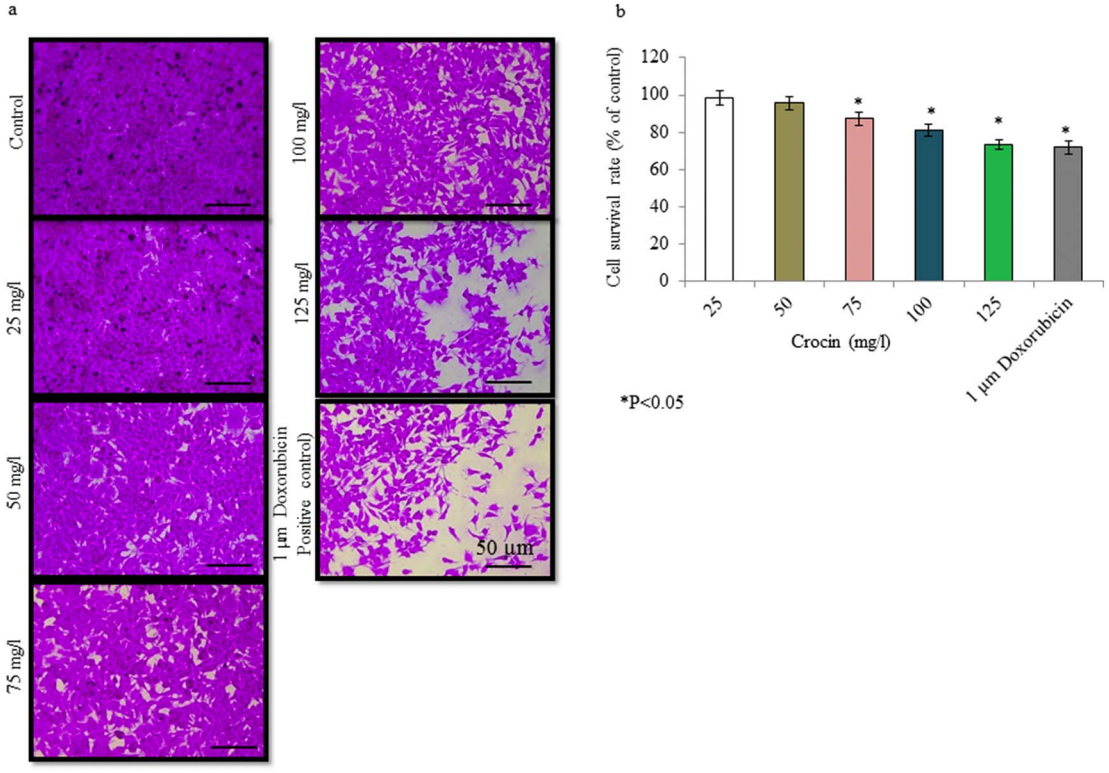

Fig. 1. Anticancer activity of crocin against human cervical carcinoma cells (a). Cell survival rate was calculated with reference to control and expressed as a percentage (b). Scale bar is 50 µm.