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# Protective Effect of *Salacia Oblanga* and *Quercetin* on Cyclophosphamide-Induced Chromosome Aberrations in Rat Bone Marrow Cells

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*Abstract: Medicinal plants, especially rich in polyphenolic compounds, have been suggested to be chemopreventive on account of antioxidative properties. Salvia officinalis L., an aromatic and medicinal plant, is widely used in folk medicine and is well known for its antioxidant properties. Therefore, the present study was designed to investigate the possible genotoxic, and oxidative stress potency Salacia oblanga and quercetin against cyclophosphamide (CP) in Wistar albino rats. Rats were administered orally Salacia oblanga: SO (3g/kg/day) and Quercetin: QE (50 mg/kg/day) for 15 days. After the same doses of SO and QE given for 15 days, rats were intraperitoneally administered CP (40 mg/kg) on days 14 and 15 of the experiment. Toxicity evaluation was carried out as a mutagenicity test i.e., chromosomal aberrations (in-vivo) with pharmacotoxic symptoms observed, as drug induced toxicity was not observed in chromosomal structural changes especially pulverization and polyploidy. Root bark extract of (Methanolic 80%) Salacia oblanga was found to be safe at the dose of 3 g/kg b.wt, administered orally for 15 days, and the results compared with Quercitin and the positive control cyclophosphamide, a known mutagenic compound. Genotoxic effects were examined in bone marrow, followed the LPO and GSH oxidative damage in liver tissues evaluated. Significant decreases in the levels of antioxidant enzymes (superoxide dismutase, catalase and glutathione peroxidase), reduced glutathione and mitotic index were observed. QE completely and SO partly decreased chromosome aberrations and aberrant cells compared to CP alone.*

*Results from the current study suggested that QE and SO supplementation attenuates CP induced genotoxicity through a mechanism related to their ability to decrease oxidative stress and inflammation, In addition, SO and QE may play a role in reducing cytogenotoxicity induced by anti-neoplastic drugs during cancer chemotherapy.*

*Keywords: Methanolic extract of root bark Salacia oblanga (80%), quercetin, cyclophosphamide, chromosomal aberrations, pulverization and polyploidy.*

## I. INTRODUCTION

Cyclophosphamide (CP) is an alkylating agent and its tumor cell-killing activity is mainly due to its DNA alkylation. Phosphoramide mustard and acrolein are the two active metabolites of CP. CP metabolites can react with carboxyl (-C [O] OH), mercapto (-SH), amino (-NH2), phosphate (-PO3H2) and hydroxyl (-OH) groups, and can form cross-links with DNA and proteins (Todorova et al., 2009). The precise mechanism by which CP causes toxicity is unknown; however numerous studies have shown that CP exposure can disrupt the redox balance of tissues, suggesting that biochemical and physiological disturbances may result from oxidative stress. Accordingly, the toxic effects of CP on cardiac tissues (Mythili et al., 2005; Senthilkumar et al., 2006; Todorova et al., 2009; Motawi et al., 2010; Nagi et al., 2010) and hemorrhagic cystitis (Bhatia et al., 2006; Linares-Fernández and Alfieri, 2007; Bhatia et al., 2008; Arafa, 2009; Motawi et al., 2010; Santos et al., 2010) were demonstrated in different animal models. Furthermore, in somatic cells, CP has been shown to produce gene mutations, DNA-strand breaks, chromosome aberrations (CA), micronuclei and sister chromatid exchanges in a variety of cultured cells (Bussing et al., 1995; Selvakumar et al., 2006). *Salacia oblanga* widely used as a hypoglycemic agent, rheumatism, gonorrhoea, itches, asthama, thirst and ear diseases in traditional medicine ((Anonymous, 1972. Andersson M A, 2007. Ashok K.G, 1996).

The isolated chemical constituents are Salacinol, Kotalanol and Fridelone – type triterpene, kotalogenin – 16 – acetate (Choudhury A.R. 1997). Chromosomal aberration study in-vivo and cyclophosphamide is used as a positive control (Chauhan L K, 2007. Evans, H.J. 1976). Mutagenic compound (Galloway.S.M,1994). The dietary supplements of mustard oil and garlic extract are reduced the clastogenic effects of sodium arsenite closer to the level of the negative control. The greater efficacy could be due to the radical scavenging activity (Giri AK, 1989).

Quercetin (QE) is a flavonoid present in many vegetables, fruits and beverages. Due to its anti-oxidant, anti-tumor and anti-inflammatory activity, QE has been studied extensively as a chemoprevention agent in several cancer models (Jeong et al., 2009). In addition quercetin minimized the toxic effects of CP on bladder by reducing inflammation (Pincemail et al., 1988) and oxidative stress (Ozcan et al., 2005). The current study is the planned on the anticytotoxic and antigenotoxic effects of SO & QE on CP in bone marrow cells *in vivo.* QE (Farombi and Onyema, 2006; Attia, 2010; Gupta et al., 2010) possess antigenotoxic/antimutagenic activity and reduce the clastogenic effects of antitumor agents.

The clinical efficacy of CP is restricted due to its toxic effects in normal cells. Therefore, it is important to prevent the oxidative stress and DNA damage induced by CP in normal cells in clinical applications. The experimental end points included enzymatic superoxide dismutase (SOD), catalase (CAT), and nonenzymatic antioxidant glutathione (GSH) pro-oxidant enzymes; lipid peroxidation (LP) measurement for the determination of oxidative stress and inflammation. Genotoxicity end points included evaluation of mitotic index (MI) and chromosomal aberration (CA) in the bone marrow of Rat.

## II. Materials and Methods

The root-bark extract of *Salacia oblanga* was collected from the Ankola, Karwar district, Karnataka State, India – the tropical rain forest area in February 2012 and it was processed (Augusti KT, 1995. August KT. 1973), by the Biotechnology department, where the voucher specimens (BT/170, 80%-vacum tray dried) are deposited. Methanolic extract of *Salacia oblanga* root bark (80%) served as Treatment groups in rat at a dose level of 3gm/kg.bwt and Quercetin: QE (50 mg/kg/day) for 15 days and Cyclophosphamide as Positive control as a single dose of 40mg /kg – IP, on $15^{th}$ day in an ambiguient and hygienic lab setup. All these 4 groups of animals observed daily for pharmacotoxic, pathological symptoms and mortality in this study. This test is used to screen for possible mammalian mutagens and carcinogens, this in vivo mammalian cytogenetics test referred to be the basic EPA OPPTS Test Guidelines (OECD 475) – OPPT 40 CFR 798, 5385. For pre clinical studies this *in vivo* mutagenecity test is a must to establish the safety of the plant extracts (Galloway, S.M. 1987). On the last day of the experimental analysis the test animals were sacrificed prior to that they are treated with a metaphase – arresting substance i.e. Colchicines and the bone marrow is collected and aspirated in neutral Phosphate buffer saline, followed by slide staining and microscopic analysis for Chromosome aberrations.

**The following parameters were kept under stringent observation:**

Gap is an achromatic lesion smaller than the width of one chromatid, and with minimum misalignment of the chromatid (s). Mitotic index will be the ratio of cells in metaphase divided by the total number of cells observed in a population of cells; an indication of the degree of proliferation of that population. Polyploidy is a multiple of the haploid chromosome number (n) other that the diploid number (i.e., 3n, 4n, and so on). Structural aberration is a change in chromosome structure detectable by microscopic examination of the metaphase stage of cell division, observed as deletions and fragments (Pulverization), intrachanges, and interchanges. The mitotic index as determined as a measure of cytotoxicity in 1,000 cells / animal for the both experimental groups.

***Drugs and chemicals:***

Cyclophosphamide and Quercetin, was purchased from HIMEDIA labs – Mumbai, India, colchicines (S.D Fine Chem) and all other chemicals and reagents are analytical grade.

**Animals and treatment:**

The study was approved by the Institute *Animal Care Ethics Committee* obtained from the Central Animal facility, Sri Raghavendra Enterprises. Bangalore. India (Reg. no. 854/9/12/ CPCEA), were used for the study. Laboratory bred Wistar albino rats of both sexes weighing between 150 and 200 gm were housed in polypropylene cages at a population density of six per cage, under controlled environmental conditions of t

emperature ($27 + 30^0$C) with normal pellet diet and water was provided ad libitum

For the control group (C) a total of 1 mL/kg of 0.9% NaCl solution was administered orally by intragastric intubation at the same time every day for 15 days until the mice were euthanized. Methanolic extract of SO (3g/kg/day) and QE (50 mg/kg/day) were administered orally by gastric gavage for 10 days in the VA and

QE groups, respectively. Cyclophosphamide was administered (40 mg/kg/day, i.p) on days 8 and 9 of the experiment in the CP group. VA and QE were given in combination with CP, as per the CP+VA and CP+QE groups, respectively.

**Sample collection and preparation**

Immediately after being removed from each animal, the Liver tissues were rinsed thoroughly in cold phosphate-buffered saline (PBS). The homogenates were centrifuged at 5000 x g for 30 min at 4˚C and supernatants were used for LP and GSH assays.

**Measurement of reduced glutathione, lipid peroxidation:**

Tissue levels of GSH were determined by the method described by Moron et al. (1979). It reacts with 5.5 0-dithiobis–2-nitrobenzoic acid to form 5-thiobis–2-nitrobenzoic acid which was detected spectrophotometrically at 412 nm. The extent of lipid peroxidation was determined by the method of Esterbauer and Cheeseman (1990). One of the markers for LP is the production of malondialdehyde (MDA). The LP level in the samples was calculated by using the extinction coefficient of MDA which is $1.56\times105\ M{-}1\ cm{-}1$. Protein content was assayed by employing the method of Lowry et al. (1951) using bovine serum albumin as the standard.

**Mitotic index and chromosomal aberrations analysis:**

Six animals in each group were used for the CA analysis. Cytogenetic analysis of bone marrow cells was carried out according to Preston et al. (1981). Animals were administered an aqueous solution of 2 mg/kg colchicine 2 hr before scheduled euthanasia by cervical dislocation. Both femurs were dissected out and cleaned of any adhering muscle. Bone marrow cells were collected from both the femurs by flushing in isotonic, 0.9% NaCI. The cells were centrifuged at 1200 rpm for 10 min and the pellet was re-suspended in 0.56% KCl and incubated at 37°C for 25 min. Cells were re-centrifuged at 1200 rpm for 10 min and then fixed in chilled Carnoy's fixative (acetic acid: methanol. 1:3. v/v) three times. Fixed cells were re-suspended and dropped onto chilled slides, flame-dried and stained on the following day in 5% buffered Giemsa at pH 6.8. Slides were examined using a Labomed light microscope at 100X magnification. MI was calculated by scoring metaphase cells from 1000 interphase nuclei per animal. CA were calculated from one hundred, well spread, intact metaphase cells per animal and classified according to Savage (1976). The number of each type of aberration, the mean of CA and cells with aberrations were recorded and summarized.

**Statistical analyses:**

Results are expressed as mean ± SD. All statistical comparisons were performed by using one-way analysis of variance (ANOVA) followed by Tukey's HSD multiple comparison test. The computer program (SPSS 12) was used for all procedures and $p < 0.05$ was regarded as statistically significant.

## III. Results

As methanolic extract of *Salacia oblanga* root bark (80%) treated animals (rat) did not showed any pharmacotoxic, pathological symptoms and mortality. The mitotic index as determined as a measure of cytotoxicity in 1,000 cells / animals. Where in pulverization and polyploidy considered as preliminary parameter before analyzing chromosomal and chromatids breaks and gaps, since there is no structural – Deleterious effects observed in rest of the animals but except positive control Cyclophosphamide group (4.65 ± 0.67). Cyclophosphamide used as known *clastogen* which induces metabolic activation. The mitotic index was calculated by the formula

$$MI\ \% = \frac{\text{Metaphase plate}}{\text{Blast cells}} \times 100$$ (Galloway, S.M. 1987)

To evaluate genotoxicity, and mitotic index and cell proliferation kinetics were used as parameters for cytostatic and cytotoxic ability (Heddle JA. 1973). An increase in polyploidy / pulverization may indicate that the test substance has a potential to induce numerical chromosome aberrations (Huang Y.1983, Jenniffer, A, 2007). The anthraquinone sennoside B and rhein were showed weakly genotoxic (Karunanayake EH. 1984). Results for chromosomal aberrations tabulated in Table I.

**Table I: Chromosomal aberration analyses in Rat bone narrow (% aberrations) in vivo.**

| Groups | Total cells counted | Number of chromosomes | Pulverization (%) | Mitotic index (%) |
|---|---|---|---|---|
| Normal control | 1235.6 ± 94.3 | 24 = 40 | NAD | 16.10±1.23# |
| Positive control Cyclophophamide (40 mg/kg : | 1573 ± 185 | 24 = 40 | 4.65 ± | 7.27 ± 0.93* |

| | | | | |
|---|---|---|---|---|
| IP single dose) | | | 0.672 | |
| Salacia oblanga+ CP treated (oral) 3g/kg/b.wt (15 days) | 1201 ± 48 | 24 = 40 | NAD | 15.25 ± 0.65• |
| Quercetin + CP treated (oral) 50mg /kg/b.wt (15 days) | 1046 ± 26 | 24 = 40 | NAD | 14.12 ± 0.50• |

NAD – No Abnormalities Detected
Statistical significance: *# $p < 0.008$, *• $p < 0.002$

Both LPO and GSH activity, where there was a significant difference ($p<0.05$) for the SO treated group, (Table 2). The intraperitoneal administration of a total of 80 mg/kg of CP 48 h prior to the termination of the experiment caused a significant ($p<0.05$) decrease in antioxidant enzyme activities (CAT, SOD, GSH).

**Table: 2** The Effect of *Salacia oblanga* extract (SO) and Quercetin (QE) on Cyclophosphamide (CP)-Induced Alterations in Lipid Peroxidase (LPO): expressed as MDA (µM/g protein), CAT (k/g protein), and SOD (U/g protein) activities in rat liver (n = 6 per group). Values are expressed as mean± standard error. In each row, values with different superscripts indicate a significant difference ($P < 0.05$).

| **Groups** | **LPO** | **GSH** | **Protein (µg/ml)** | **MDA** | **CAT** | **SOD** |
|---|---|---|---|---|---|---|
| **Control** | 48.1 ± 5.2 | 1.2 ± 2.0 | 56 ± 4.2 | 18.26±0.68 | 92.74±2.40 | 124.12±1.76 |
| **Quercetin + CP** | 45.7 ± 4.9 | 1.3 ± 0.2* | 52 ± 4.0 | 32.60±0.46 | 42.54±1.60 | 90.24±1.84 |
| ***Salacia oblanga* + CP** | 54.0 ± 6.0 | 1.4 ± 0.4 | 58 ± 6.2 | 28.50±0.24 | 54.20±1.32 | 102.26±1.72 |
| **Cyclophosphamide** | 82.8 ± 8.9 | 0.8 ± 0.2* | 42 ± 3.4 | 16.08±0.69 | 96.40±2.50 | 132.42±2.50 |

SO and QE were given orally to Rats 3g/kg and 50 mg/kg/day, respectively for 15 consecutive days and CP (40 mg/kg; i.p.) was administered on the fourteenth and fifteenth days. Results are expressed as U/mg protein for CAT, SOD, and CAT: µmoles $H_2O_2$ decomposed min−1 mg−1 protein; SOD: 50% inhibition of nitroblue tetrazolium min−1 mg−1 protein; GSH-CDNB conjugate formed min−1 mg−1 protein; respectively. Data are the mean ± SD of 6 Rat. * < 0.05: Compared with control, difference is statistically significant, # < 0.05: Compared with CP group, difference is statistically significant.

**Table 3:** Mitotic Index, Distribution of the Different Types of Chromosomal Aberrations and Aberrant Cells Observed in Mouse Bone Marrow Pre-Treated with *Salacia oblanga* (SO) Extract and QE, Alone or in Combination with Cyclosphamide (CP)

| **Compounds** | **MI (Mean ± SD)** | **P** | **SCU** | **B'** | **B"** | **F** | **CF** | **Total -CA** | **CA** | **Aberrant Cells** |
|---|---|---|---|---|---|---|---|---|---|---|
| **Control** | 72.6±12.1* | 1 | 2 | 2 | - | - | - | 8 | 1.6±0.8 | 1.6±0.8* |
| **Quercetin + CP** | 63.8±5.4* | 5 | 1 | 1 | - | 6 | 1 | 14 | 2.8±1.0 | 2.8±1.0* |
| **Cyclophospha-mide** | 37.1±11.3* | 16 | 12 | 34 | 8 | 10 | 7 | 141 | 28.2±8.1 | 23.8±6.1* |
| ***Salacia oblanga* + CP** | 63.8±5.4* | 5 | 1 | - | - | 6 | 1 | 14 | 2.8±1.0 | 2.8±1.0* |

MI: Mitotic index; CA: Chromosomal aberrations; P: Polyploidy; SCU: Sister chromatid unions; B': Chromatid breaks; B'': Chromosome breaks; F: Fragments; CF: Centric fusions; CE: Chromatid exchanges.
Data are the mean ± SD of 6 rats. * < 0.05: Compared with control, difference is statistically significant, when compared with CP group.

The effects of *Salacia oblanga* (SO) and CYP on the levels of lipid peroxidation in rat liver, are shown in the Table.2. CYP treatment led to a significant increase in MDA levels in all groups as compared to the

control group. Despite this, significant restoration in the MDA profile was observed in animals that received *Salacia oblanga* (SO) as compared to animals that received only CYP. As shown in the Table, the activity of SOD in liver tissue homogenates was significantly decreased in CYP-treated rats when compared with the control. Oral administration of methanolic extract *Salacia oblanga* (SO) showed a significant increase in SOD activity in all tissues of CYP-treated rats as compared to animals that received only CYP.In CYP-treated groups, CAT levels were significantly decreased in all tissues as compared to the control animals. In the pretreatment groups receiving the methanolic extract of *Salacia oblanga* (SO) prior to CYP, CAT activity was significantly increased in liver tissues. The bone marrow chromosomal aberration assay is the widely used test to assess the clastogenic/aneugenic potential of chemicals.

Table 3: summarizes the effects of SO extract and QE, in combination with CP on the MI and CA in rat bone marrow cells. As expected, CP treatment significantly decreased the MI and induced CA and aberrant cells ($P<0.05$). CP-induced CA consisted mainly of fragments, chromatid breaks and sister chromatid unions. No significant difference in MI values was observed between the animals that received the SO or QE alone or in combination with CP, compared to the control. Pre-treatment with SO and QE improved the mitotic activity against CP. CA and aberrant cell counts were found to significantly decrease compared to CP alone ($p<0.05$).

## IV. Discussion

*Salacia oblanga* extract lowers acute glycemia and insulinemia in persons with type 2 diabetes after a high-carbohydrate meal. Other research work results suggested that *Salacia* may be beneficial for postprandial glucose control (Locke-huhle C. 1983). In one of the Toxicological work, (-) - Hydroxycitric acid (HCA) is widely used as an ingredient for nutritional supplements aimed at reducing food intake, appetite, and body weight. In an *In vitro* chromosomal aberration (CA) test, HCA preferentially induce micronuclei (Lee K H, 2007).In another research work, Fumagillin is a naturally secreted antibiotic of the fungus Aspergillus fumigatus. It is used in veterinary medicine against microsporidiosis of bees and fish. Evaluated in mouse bone-marrow cells using the mitotic index (MI) and the chromosome aberration (CA) assay parameters. When the results showed significantly increased frequencies structural chromosomal aberrations such as gaps, breaks, and centric rings, which were observed at the highest experimental dose of fumagillin (75 mg/kg b.wt) compared with the negative control. Fumagillin has genotoxic (clastogenic) potential in mammals in vivo (Matsuda H, 1979).Chromium picolinate (Cr-Pic) is a synthetic nutritional supplement primarily used for weight loss and muscle building. In a high concentration of Cr-Pic showed DNA damaging, but only under non-physiological conditions (Mutsuoka, 1979).

The cytogenetic effects of deltamethrin (DEL) showed a significant frequency of CA at 10 micro M. Findings indicate that the in vitro and in vivo exposure of a commercial formulation of deltamethrin can cause genotoxic effects in mammals.This study conducted to establish safety data's for *Salacia oblanga* on chromosomal aberration test as a mutagenicity study in-vivo with cyclophosphamide induced Bone narrow in mice. The results indicated that there is no drug-induced cytotoxicity at the dose of 3g/kg b.wt, for 15 days treatment in mice. At this dose the root bark extract of *Salacia oblanga* (Methanolic extract 80%) seems to be safe.GSH is a key regulator of the cellular redox state and the redox environment within the tumor cells determines the response of tumors (and protection of the normal cells) to chemotherapy and radiation (Todorova et al., 2009). CP-induced decrease in GSH level and increased lipid peroxidation were demonstrated in cardiac tissue in previous studies (Mythili et al., 2005; Senthilkumar et al., 2006; Todorova et al., 2009; Nagi et al., 2010). The increased antioxidant enzyme activities may reflect an improved antioxidant status of animals pretreated with QE or VA, as indicated by elevation of GSH level and reduction in LP. This changes may be may militate against CP-induced cell damage and oxidative stress. Earlier studies revealed that QE prevented changes in heart mitochondrial enzyme activities and damage to the outer mitochondrial membrane in animals after daunorubicin application (Guzy et al., 2003).QE not only has a proven antioxidant effect *in vitro* and *in vivo*, but it may also stimulate glutathione synthesis by modulating gene expression of glutamylcysteine synthase (Moskaug et al., 2005).

A possible explanation for the observed physiological and biochemical effects of SO have been attributed to its phytoconstituents, especially those having antioxidant activity, such as the phenolics. The antioxidant activity of phenolics is due to their redox properties which allow them to act as reducing agent, metal chelators and free radical scavengers (Rice-Evans et al., 1996). The antioxidant properties of methanolic extracts of SO have also been demonstrated in previous studies (Onay-Ucar et al., 2006; Oluwaseun and Ganiyu, 2008).A relationship between genotoxicity and oxidative stress has been well demonstrated in many experimental animal models. Many authors found that genotoxicity and chromosomal instability induced by many agents are directly correlated with the parameters of oxidative stress . Numerous studies have demonstrated that ROS such as superoxide, hydroxyl radical anion, and hydrogen peroxide are important mediators of DNA damage and tissue injury. SOD and CAT are the important antioxidant enzymes of cell defense against free radical damage. SOD constitutes an important link in the biological defense mechanism

through dismutation of endogenous cytotoxic superoxide radicals to H2O2 and molecular oxygen, which are deleterious to polyunsaturated fatty acids and proteins. CAT is hemoprotein, which catalyzes the reduction of hydrogen peroxides and is known to be involved in the detoxification of H2O2 concentrations.In the present study the activities of SOD and CAT decreased in CYP treated rats as reported earlier, which could be due to inactivation of cellular antioxidants by the lipid peroxides and ROS that are produced due to CYP intoxication.

However, pretreatment with the *Salacia oblanga* extract restored the enzyme levels and decreased the formation of lipid peroxidation byproduct MDA. The restoration of oxidative stress by improving the antioxidant defense system might be ascribed to the free radical scavenging/antioxidant properties of the phytochemical constituents present in *Salacia oblanga*. There is increasing evidence that a plethora of plant components such as flavonoids, Terpenoids, polyphenolics, carotenoids, catechins, and plant steroids can act as inhibitors of mutagenesis. It is known that chemoprotective agents are capable of exerting their antigenotoxic effects by a single mechanism or a combination of mechanisms. These mechanisms include the scavenging of ROS, the inhibiting of formation of reactive carcinogenic metabolites, the inducing of carcinogen-detoxifying enzymes, and the influencing of apoptosis and inhibiting of cell proliferation. Several reports indicated that the compounds responsible for antioxidative activity of *Salacia oblanga* mainly phenolic acids and flavonoids, Salacinol, Kotalanol and Fridelone – type triterpene, kotalogenin – 16 – acetate (Choudhury A.R. 1997). *Salacia oblanga* and its phenolic compounds have been shown to have protective effects against oxidative stress.

Although CP affects virtually every organ system in the body, the cell populations that typically exhibit rapid cell turnover such as those of the bone marrow and gastrointestinal mucosa, are the most sensitive (Selvakumar et al., 2006). As expected, mice treated with CP in the present study showed a significant decrease in MI and increases in CA and aberrant cells in bone marrow cells when compared to the control group. The improvement in mitotic activity of bone marrow cells of animals pre-treated with SO and QE may further focus attention on the beneficial effect of these substances in overcoming two of the most serious problems in cancer chemotherapy, which are bone marrow suppression and related immunosuppression. Similar observations related to the antigenotoxic/antimutagenic effects of QE (Farombi and Onyema, 2006; Attia, 2010, Gupta et al., 2010 and VA (Kuttan et al., 1990; Bussing et al., 1995; Kovacs, 2002) have been reported.

To conclude the antioxidant defense system SO and QE were effective in alleviating the oxidative injury to the liver imposed by CP, the genoprotective effects of SO extract are due mainly to the antioxidative effects of the respective compound quercetin. These beneficial effects of quercetin in the present study seemed almost comparable with those obtained with SO extract, this is probably due to better absorption of QE in comparison to SO or alternatively, and the antioxidant capacity of SO extract at 3g/kg /day is less than that of pure phenolic QE at 50 mg/kg /day. The improvement in animals pretreated with SO and QE may focus attention on the beneficial effect of these substances to overcome one of the most serious problems in chemotherapy.

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