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Original Article

Assessment of the antigenotoxic activity of white sesame extract *(Sesamum indicum)* against vincristine induced genotoxicity in mice

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Abstract

White sesame seeds, used as an oilseed since ancient time, contain 25% protein and 50% oil, the latter have unique chemical and physiological activities. Considering its important biological activity, this study was performed to evaluate the efficacy of sesame oil (SO) to protect mice against vincristine (VCR) induced genotoxicity using different endpoints. Chromosomal aberrations (CAs) in bone marrow cells and in spermatocytes as well as morphological sperm abnormalities were determined in tested animals. Mice were orally treated (using a stomach tube) with SO for 7 consecutive days. Vincristine was used as a mutagenic agent and it was given intraperitoneally at a single dose of 0.5 mg/kg b.w, 24 h after last dose of SO. The results clearly showed that SO tested at high dose (400 mg/mouse) did not induce any genotoxic effect. Pretreatment with the three tested doses of SO (100,300 and 400 mg/mouse) to VCR-treated mice significantly minimized CAs in bone marrow cells and spermatocytes. Morphological sperm abnormalities decreased significantly after treatment with SO. It could be concluded that, intake of dietary SO may be considered a promising approach toward reducing the genotoxicity induced by chemotherapeutic agent VCR. Accordingly, sesame seeds and their components may be exploited commercially for pharmaceutical purposes.

Keywords: Chromosomal aberration, bone marrow cells, spermatocytes, sperm abnormality

Avaliação de atividade antigenotoxica de extrato de gergelim branco (Sesamum indicum) versus a genotoxicidade induzida por vincristina em camundongos

Resumo

Sementes de gergelim branco, usado como uma oleaginosa desde os tempos antigos, contêm 25% de proteína e óleo de 50%, este último tem química única e atividades fisiológicas. Considerando-se tendo em vista a sua actividade biológica importante, este estudo foi realizado para avaliar a eficácia de óleo de gergelim (SO) para proteger camundongos contra a genotoxicidade induzida vincristina (VCR) utilizando parâmetros diferentes. Aberrações cromossômicas (CAs) em células da medula óssea e em espermatócitos, assim como anormalidades no esperma morfológicas foram determinadas nos animais testados. Camundongos foram tratados por via oral (utilizando um tubo estomacal) com SO durante 7 dias consecutivos. Vincristina foi usada como um agente mutagênico e foi dado intraperitonealmente com uma dose única de 0,5 mg/kg de peso corporal, 24 horas após a última dose de SO. Os resultados mostraram claramente que SO testados em alta dose (400 mg/rato) não induziu qualquer efeito genotóxico. Pré-tratamento com as três doses testadas de SO (100,300 e 400 mg/rato) para VCR camundongos tratados significativamente minimizado CAs em células de medula óssea e de espermatócitos. Anormalidades morfológicas de espermatozóides diminuiu significativamente após o tratamento com SO. Poderia-se concluir que, a ingestão dietética de SO pode ser considerada uma abordagem promissora para a redução da genotoxicidade induzida por quimioterápicos agente VCR. Assim, sementes de gergelim e os seus componentes podem ser exploradas comercialmente para fins farmacêuticos.

Palavras-chave: Aberração cromossômica, medula óssea, espermatócitos, anormalidade no esperma

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Introduction

Chemotherapy is routinely used in the treatment of various types of cancer and it has become indispensable in the current medical management of malignant tumors. However, most of cancer chemotherapeutic agents are mutagenic and carcinogenic, and non-target-specific, meaning, they affect all body cells and tissues that they encounter, particularly the tissues with rapid cell division (Mladosievicova et al., 2007).

Vincristine (VCR) is a dimeric alkaloid isolated from the periwinkle plant *Catharanthus roseus*. VCR has been widely used to treat the paediatric leukemias, solid tumors and hematological malignancies as a standard component of chemotherapeutic regimens, owing to its comparatively mild myelosuppressive action (Jagetia & Baliga, 2002). However, VCR also was listed as one of the 10 anticancer agents which were classified into group I carcinogens (carcinogenic to humans) by IARC (Sorsa & Anderson, 1996). A number of *in vivo* and *in vitro* studies have shown that VCR can induce the high frequencies of micronuclei (Hongping et al., 2006; Cammerer et al., 2007), chromosomal aberrations (Arni & Hertner, 1997; Yamada et al., 2000) and sister chromatid exchanges (Trenz et al., 2003). Also, VCR can produce DNA damage (Tiburi et al., 2002; Wei et al., 2008).

Sesame (*Sesamum indicum*) is one of the most important oilseed crops. It is a source of edible oil and it provides a nutritious food for humans. Sesame oil is highly stable towards oxidation compared with other vegetable oils, because of the presence of sesamin, sesamolin, sesaminol, and γ-tocopherol (Fukuda et al., 1996).

Many bioactivities have been assigned to sesame seeds, such as antioxidant (Ikeda et al., 2003), antidiabetic (Takeuchi et al., 2001), antihypertensive (Noguchi et al., 2001), antihepatotoxic (Kapadia et al., 2002), antiinflammatory (Mosayebi et al., 2007), neuroprotective (Jamarkattel-Pandit et al., 2010), hypocholesterolemic (Chen et al., 2005), antiproliferative (Yokota et al., 2007), antimutagenic (Kaur & Saini, 2000; Lazarou et al., 2007), and angiogenic (Chung et al., 2010) activities. Furthermore, sesame ingestion (50 g sesame seed powder daily for 5 weeks) positively affected sex hormones in postmenopausal woman (Wu et al., 2006).

White sesame was chosen for our experiments with mice since it has a broad range of applications, ranging from nutritious food and cosmetics to medicine . Therefore, the evaluation of a possible mutagenic activity of sesame is important to guarantee its safe use in humans. As part of our ongoing research regarding the biological activities of plant products, we studied the potential mutagenic effect of sesame and its influence on the mutagenicity induced by the chemotherapeutic agent VCR in male mice.

Materials and Methods

Animals

Male Swiss mice (*Mus musculus*), 6–8 weeks old and weighing approximately 25–30 g, were supplied by Animal House of the National Research Center, Dokki, Cairo, Egypt. Mice were housed in polycarbonate cages with wood chip bedding and steel-wire tops, maintained in an experimental room under controlled conditions of temperature (22±2◦C), humidity (50±10%) and photocycle of 12h:12h light and dark. The animals were kept on standard mice chow and water *ad libitum*.

Test chemicals

Vincristine sulfate (Vinracine©, Korea United Pharmaceuticals) was used at the dose 0.5mg/kg b.w. based on its effectiveness in inducing chromosome damage (Choudhury et al., 2000). The drug was dissolved in 0.9% NaCl saline solution before injection.

White sesame seeds (*Sesamum indicum*) were purchased from the local market, Dokki, Cairo, Egypt. Based on previous reports (Krishnamurthy& Neelaram, 1987; Satchithanandam et al., 1996) on feeding mice on standard diet mixed with white sesame seeds (5 -20%), we have gotten as a result a good suppression of toxic effect of some chemical. It is noteworthy, average food intake of control mouse (25g) was 3.7 + 0.1g/day (Bachmanov et al., 2002).

Sesame extract was used at three different doses 100, 300, 400 mg/mouse. These doses equivalent to n-hexane extract of 0.19, 0.56 and 0.75 g sesame seeds which correspond to diet containing 5,15 and 20% sesame seeds that mouse fed daily respectively.

Oil extraction

White sesame seeds were ground into powder by a mortar grinder. Sesame powder (250g) was covered by *n*-hexane and left for three days at room temperature. The sample were stirred every 10 min to ensure a well-mixed extraction. The process of extraction was repeated three times. The extracted oil (133 g) was obtained by removing *n*-hexane in vacuo by a rotary evaporator (Hu et al., 2004).

Experimental design

Sesame oil (SO) for 7 consecutive days, at doses of 100, 300 or 400 mg/mouse through oral intubation (p.o.). Vincristine (VCR) was used as a mutagenic agent and it was given as intraperitoneal (i.p.) injection at a single dose of 0.5 mg/kg b.w., 24 h after last dose of sesame oil on the seventh day. Animals were randomly divided into six groups (5mice/group): (I) Control –Saline solution; (II) SO 400; (III) SO 100+VCR; (IV) SO 300+VCR; (V) SO 400+VCR; (VI) VCR.

For chromosomal aberration analysis, thirty mice (5mice/group) were sacrificed by cervical dislocation 24 h after VCR injection.

For sperm abnormality analysis, ninety mice were killed 1, 3 and 5 weeks after treatment and their sperm were examined. Time

interval schedule used was chosen for sampling sperm representing samples of pre-meiotic (5 weeks) and post-meiotic (1-3 weeks) stages of spermatogenesis. The sperm thus will be derived from cells exposed during spermatogenesis as spermatozoa (1week), spermatids (3 weeks) and spermatocytes (5 weeks) (Oakberg, 1984).

1-Chromosomal aberration assay in somatic and germ cells

Bone marrow chromosomes were prepared according to Julian et al., (1987), while spermatocytes chromosomes were prepared form the testes of the same animals according to Russo (2000). The slides were stained with phosphate buffered Giemsa. At least 100 well spread metaphases were examined for each somatic and germ cells for each mouse. Both structural and numerical aberrations were recoded.

2-Sperm abnormality assay

The epididymis excised and minced in 2 ml tri-sodium citrate (2.2%), dispersed and filtered to exclude large tissue fragments. A suspension was thus prepared by re-pipetting. The suspension was dropped on clean slides to make a smear. The slides were dried and stained with 1% aqueous solution of Eosin Y. At least, 1000 sperm were counted for each mouse scoring different types of sperm abnormalities according to the criteria of Wyrobek & Bruce (1975).

Statistical analysis

The data were statistically analyzed by using one-way analysis of variance ANOVA followed by Duncan's multiple range test. A value of $p<0.05$ was considered to be significant. Dose-response relationships were determined from the correlation and regression coefficient for the percentage of abnormal cells. All computations were made by employing the statistical package software (SPSS, version 11). The suppression of mutagenicity was calculated according to Hu et al. (2005) using the following formula

A: represents groups treated with VCR alone

B: represents groups treated with VCR + SO

$$\text{Suppression (\%)} = \left[\frac{\text{\% aberrant cells in group A - \% aberrant cells in group B}}{\text{\% aberrant cells in group A}}\right] \times 100$$

Results and Discussion

The incidence of chromosomal aberrations (CAs) in mouse bone marrow cells and spermatocytes is summarized in Tables 1 and 2. Mice receiving only VCR displayed a significant increase in the percentage of CAs in mouse bone marrow cells and spermatocytes. Mean percentage of CAs reached to 23.60±1.36 and 21.40±1.21 compared to 4.60±0.40, 5.20±0.37 as for control groups in bone marrow cells and spermatocytes, respectively. Such percentage represents 5.1 and 4.1 fold increases as compared with that value of the control group in bone marrow cells and spermatocytes respectively. These results suggested that VCR has potential mutagenic effects in somatic and germ cells. This is explained by the fact that vincristine is metabolized in the liver by cytochrome P-450 (CYP) dependent enzymes especially CYP3A to an active metabolite that bind to macromolecules in the target tissue to exert their mutagenic effect, that process leads to the formation of free radical (Zhou-Pan et al., 1993; Chan, 1998). Our data are in line with the findings of Choudhury et al. (2000), who reported that VCR induced a statistically significant increase in the frequencies of chromosomal aberrations and micronucleated polychromatic erythrocytes in mouse bone marrow cells. Furthermore, Vinblastine and vincristine cause an arrest of mitotic and meiotic divisions to metaphase followed by cell death, which was faster after vincristine administration. Both alkaloids had a damaging effect on the rat pachytene spermatocytes (Parvinen et al., 1978)

Concerning the types of structural chromosomal aberrations induced by VCR in mouse bone marrow cells, the majority of structural aberrations induced by VCR in mouse bone cells were of chromatid type (Figure 1). This may be due to the interference of VCR with G2-phase of the cell cycle. These findings agree with Mujagic et al. (1983), who reported that VCR induced blockage in G2 phase of cell cycle and

Table 1. Effect of pretreatment with sesame oil on vincristine induced chromosomal aberrations in mouse bone marrow cells.

Treatment groups	Structural aberrations						Numerical aberrations			Abnormal metaphases		Suppression (%)
	Gap	Br /Fra	Del.	Ring	End+R.T	M A	Endo	Aneu	Poly	Including gaps Mean %± S.E.	Excluding gaps Mean %± S.E.	
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)			
I-Control	8 (1.60)	7 (1.40)	4 (0.80)	1 (0.20)	—	—	2 (0.40)	—	1 (0.20)	4.60 ±0.40 ^{a}	3.00±0.63 ^{a}	
II-SO 400	7 (1.40)	9 (1.80)	5 (1.00)	1 (0.20)	—	1 (0.20)	1 (0.20)	—	1 (0.20)	5.00±0.55 ^{a}	3.80±0.51 ^{a}	
III-SO100+VCR	8 (1.60)	16 (3.20)	19 (3.80)	5 (1.00)	3 (0.60)	2 (0.40)	3 (0.60)	—	4 (0.08)	12.00±1.05 ^{c}	10.40±0.68 ^{c}	49.2
IV-SO 300+VCR	10 (2.00)	10 (2.00)	9 (1.80)	6 (1.20)	2 (0.40)	—	2 (0.40)	—	3 (0.60)	8.40±0.60 ^{b}	6.40±0.40 ^{b}	65.3
V-SO 400+VCR	8 (1.60)	11 (2.20)	9 (1.80)	2 (0.40)	2 (0.40)	1 (0.20)	3 (0.60)	—	3 (0.60)	7.80±0.73 ^{b}	6.20±0.49 ^{b}	66.9
VI-VCR	25 (5.00)	16 (3.20)	10 (2.00)	44 (8.80)	7 (1.40)	7 (1.40)	2 (0.40)	3 (0.60)	4 (0.80)	23.60±1.36 ^{d}	18.60±1.75 ^{d}	

500 metaphase were examined in 5 mice per each experimental group; Br=Break, Fra= Fragment, Del = Deletion, End= End to End association, R.T.=Robertsonian translocation, M.A.= metaphases with more than one type of aberrations, Endo= Endomitosis , Aneu=Aneuploidy, , Poly= polyploidy; Values within the same column follow by different superscript letters are significantly different from one another (P<0.05)

Table 2. Effect of pretreatment with sesame oil on vincristine induced chromosomal aberrations in mouse spermatocytes.

Treatment groups	No. and % of metaphases with different types of chromosomal aberrations						Abnormal metaphase	Suppression (%)
	Gap and/ or Break in X-Y	X-Y univalent	Autosomal univalent	Fragment	Chain IV	M.A.	Mean %± S.E.	
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)		
I-Control	2 (0.40)	9 (1.80)	14 (2.80)	—	—	1 (0.20)	5.20 ± 0.37 [a]	
II-SO 400	—	20 (4.00)	10 (2.00)	—	—	—	6.00±0.32 [a]	
III-SO100+VCR	1 (0.20)	14 (2.80)	60 (12.00)	1 (0.20)	—	2 (0.40)	15.60±1.12 [d]	27.1
IV-SO 300+VCR	2 (0.40)	24 (4.80)	29 (5.80)	—	—	3 (0.60)	11.60±0.60 [c]	45.8
V-SO 400+VCR	2 (0.40)	11(2.20)	22 (4.40)	2 (0.40)	—	6 (1.20)	8.60±0.81 [b]	59.8
VI-VCR	2 (0.40)	22 (4.40)	73 (14.60)	—	3(0.60)	7 (1.40)	21.40 ± 1.21 [e]	

500 metaphase were examined in 5 mice per each experimental group; M.A.= metaphases with more than one type of aberrations; Values within the same column follow by different superscript letters are significantly different from one another (P<0.05)

that it was related to the inhibition of chromatin condensation.

It is remarkable that VCR produced the highest percentage of aneuploidy (0.60%) when compared to the control group suggesting its aneugenic effect. This is attributed to VCR interacts with tubulin subunits to prevent microtubule assembly, inducing abnormal chromosome segregation in dividing cells and causing aneuploidy (Novichkova et al., 2003).

The most observed structural aberrations in mouse spermatocytes were unassociated univalent (autosomal univalents 14.60%, Figure1). This result suggested that VCR had a pronounced effect on the cohesion of two homologous chromosomes forming unassociated univalent. Kocer et al. (2009) reported that, homologous chromosomes are physically held together as bivalents by crossover events and cohesion between the DNA molecules. The gradual loss of these physical connections between homologous chromosomes contributes to the high rates of unassociated univalent.

Analysis of sperm-shape abnormalities

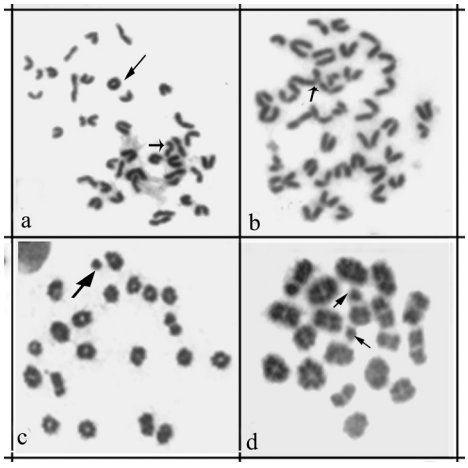

Figure 1. Metaphases plates from mouse bone marrow cells and spermatocytes after i.p. treatment with vincristine showing a) Ring and deletion b) End to end association, c) Fragment, d) Autosomal univalent.

was carried out 1, 3 and 5 weeks after the end of injection with VCR. Sperm cells observed at these periods were presumably exposed to the drug while they were spermatozoa, early spermatide and early primary spermatocytes. Table 3 illustrates that VCR induced significant increase in the percentage of sperm abnormalities compared to the negative control at all three different exposure periods of spermatogenesis. Such percentages reached 5.20±0.22, 11.90± 0.94 and 15.16±0.17 at the three different exposure periods of spermatogenesis (1, 3 and 5 weeks respectively). This result indicated that different stages of spermatogenesis have remarkable difference in their sensitivities to VCR. The induction of lower percentage of abnormal sperm after one week of treatment indicated that post-meiotic cell was less sensitive to treatment with VCR than pre-meiotic cells. The effect of VCR was more pronounced after 5 weeks post-treatment suggesting that VCR induced genetic damage in the germ cells during the early stage of sperm formation. Our data coincide with the findings of Dobrzyńska et al. (2005), who reported that VCR reduced testis weight and sperm count, caused sperm morphological deterioration and a slight increase in DNA damage. Moreover, VCR primarily affected the Sertoli cells by destroying their microtubules and mitochondria. VCR specifically damaged the acrosomic system and the cytoplasmic bridges of the young spermatids (Parvinen et al., 1978). Also, Vaisheva et al. (2007) revealed that, chemotherapy of non-Hodgkin lymphoma with cyclophosphamide, doxorubicin, vincristine, and prednisone is associated with significant gonadal damage in male mouse. Damage ranged from the presence of small vacuoles in the epithelium to tubules deprived of spermatocytes and spermatids and it was accompanied by an increased incidence of germ cell apoptosis (Vaisheva et al., 2007).

The findings illustrated that VCR induced both head and tail sperm abnormalities (Figure 2). Head abnormalities were represented by

Table 3. Effect of pretreatment with sesame oil on vincristine induced morphological sperm abnormalities in mice.

Treatment groups	Exposure periods of spermatogenesis (weeks)								
	1 week			3 weeks			5 weeks		
	Head	Tail	Total abnormality	Head	Tail	Total abnormality	Head	Tail	Total abnormality
	%	%	Mean %± S.E.	%	%	Mean %± S.E.	%	%	Mean %± S.E.
I-Control	2.56	1.10	3.66±0.36^{a}	2.72	0.98	3.70±0.38^{a}	2.78	0.82	3.60±0.40 ^{a}
II-SO 400	2.82	1.04	3.86±0.20^{a}	3.26	1.14	4.40±0.23^{a}	3.62	0.68	4.30±0.31^{a}
III-SO100+VCR	2.44	2.68	5.12±0.28^{b}	6.44	1.70	8.14±0.48^{c}	5.54	5.16	10.70±0.98^{c}
IV-SO 300+VCR	3.04	2.02	5.06±0.27^{b}	5.08	1.46	6.54±0.61^{b}	5.76	3.52	9.28±0.41^{c}
V-SO 400+VCR	2.80	1.92	4.72±0.20^{b}	4.14	0.86	5.00±0.22^{ab}	2.10	4.38	6.48±0.28 ^{b}
VI-VCR	2.06	3.14	5.20±0.22^{b}	4.46	7.44	11.90± 0.94^{d}	7.10	8.06	15.16±0.17^{d}

5000 sperm were examined in 5 mice per each experimental group; Values within the same column followed by different letters are significantly different form one another ($p < 0.05$).

a change in the shape or in the size. While, tail abnormalities were represented by a coiled tail. Accordingly, VCR induced detrimental genotypic changes in the spermatogenic cells that affect the phenotype of the sperm. It is noteworthy that, all types of abnormal sperm-head occurred with different frequencies in both, treated and control animals. There was no shift towards the different types on treated mice compared to control group.

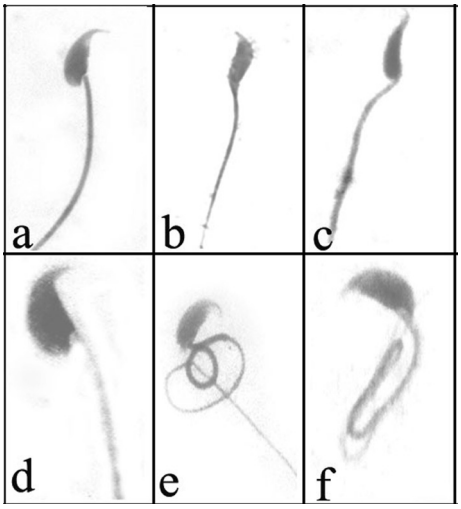

Figure2. Different type of sperm abnormalities (a) Normal; (b) Amorphous; (c) Banana; (d) Big; (e,f) coiled tail.

The percentage of tail abnormalities was based on a time-dependent relationship. It increased with the advancing of the exposure period of spermatogenesis. Its percentage reached 3.14, 7.44 and 8.06% in mice treated with VCR only at three tested periods of spermatogenesis (1, 3 and 5 weeks) respectively. This result seems to have connected VCR to insufficiency sperm maturation during epididymis transport. This view is supported by Averal et al. (1996), who reported that VCR caused conspicuous pathological changes in the principal and apical cells of the caput and in the clear cells of the cauda. Such changes point to a toxic effect of VCR on these cell types, suggesting impairment of epididymal function, particularly concerning to sperm maturation and endocytotic removal of the contents of the cytoplasmic droplets and dead sperm.

In recent years, a number of natural products of diverse structures have been found to inhibit the process of cancer development in several laboratory models (Yokota et al., 2007; Chung et al., 2010). Among these classes of natural products, great attention is being paid to the antioxidants because of their intrinsic capabilities to prevent lipid peroxidation, which is proposed to be closely related to aging, mutation, cancer and several other diseases (Satchithanandam et al., 1996).

Regarding the genotoxicity of the SO, our findings have showed that SO (400mg/ mouse) did not induce genotoxicity of its own in all the tests examined. This results are similar to the findings of Hori et al. (2011), who evaluated genotoxicity of sesame lignans (sesamin and episesamin), which are compounds commonly found in refined sesame oil. Oral administration of sesamin at doses up to 2g/kg b.w. did not cause a significant increase either in the percentage of micronucleated polychromatic erythrocytes in mouse bone marrow cells or in the percentage of DNA in the comet assay in mouse liver cells. Also, episesamin showed negative results in the Ames test, in "*in vitro*" chromosomal aberrations in cultured Chinese hamster lung cells and in "*in vivo*" comet assay in mouse liver cells. Accordingly, two compounds judged to be free of genotoxicity.

Pretreatment with SO at different doses (100, 300 and 400 mg/mouse) to VCR-treated mice significantly lowered the occurrence of CAs in bone marrow cells and spermatocytes compared with the corresponding mice treated with VCR only. Such suppression ranged from 49.2–66.9% in bone marrow cells and from 27.1–59.8% in spermatocytes. Regression analysis was performed to determine the dose effect of SO on VCR and the percentage of abnormal metaphases. A decrease in the slope of linear regression lines was observed as the dose of the SO increased, in each of bone marrow cells and spermatocytes. Such decrease demonstrated significant negative correlation between the

increase of SO dose and the decrease of percentage of abnormal metaphases suggesting presence of dose-dependent protective effect of SO (Figure 3).

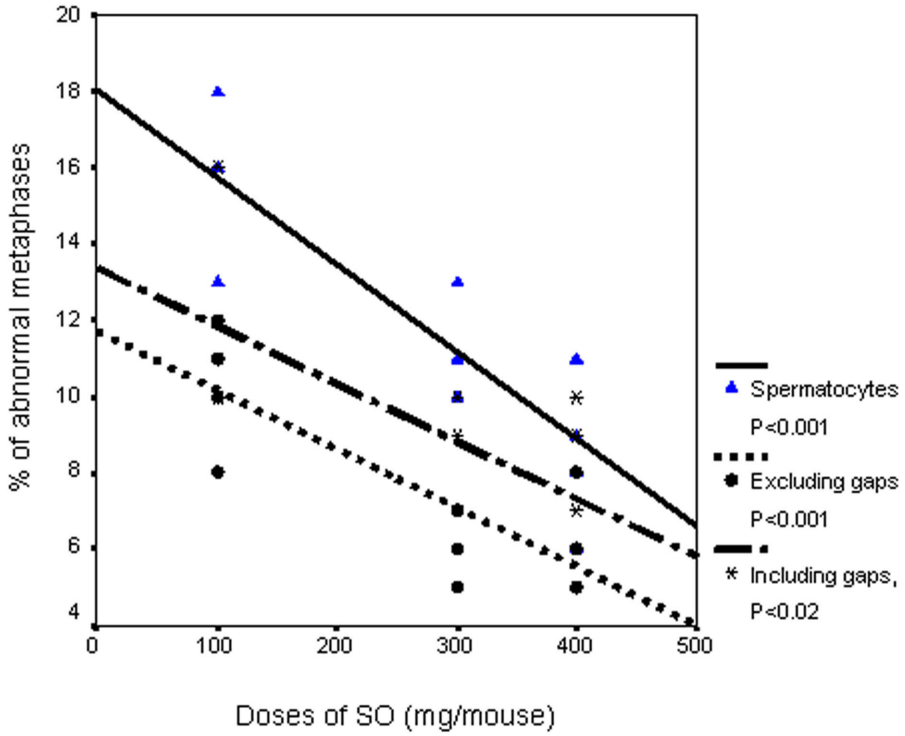

Figure 3 Linear regression analysis for the dose effect of SO on the percentage of abnormal metaphases induced by VCR. Correlation coefficients of bone marrow cells including gaps (—– –), excluding gaps (……) and spermatocytes (———) were, respectively, r=0.734 (Y=13.371–0.015X), r=0.846 (Y=11.714–0.015X)] and r=0.849 (Y=18.029–0.023X).

According to our results, it appears that SO prevent the activation of VCR metabolism, suggesting its desmutagenic effect. This view is supported by De Flora (1998), who reported that the compounds with blocking (desmutagenic) activity act preferentially when they are administered concurrently with, or, prior to the mutagen. Whereas, suppressing agents (bioantimutagens) act mostly when administered after mutagen. Kaur & Saini (2000) demonstrated that sesamol have a desmutagenic effect against tert-butylhydroperoxide (t-BOOH) induced mutagenesis in *Salmonella typhimurium* strain TA102. Also, Lazarou et al. (2007) has found that a polyphenolic mixture derived from sesame-seed perisperm (SSP) exhibited desmutagenic activity against hydrogen peroxide, and benzo[a]pyrene in TA98 and/or TA100 and biomutagenic activity against sodium azide in strain TA100 of *Salmonella typhimurium*. Considering the fact that sesame seed oil is a mixture of lignans and phenolic antioxidants, this property may be central in the intrinsic capabilities observed of cancer chemopreventive activities. According to Liu et al. (2006), lignans can be converted by intestinal microbiota to the mammalian lignans, enterodiol and enterolactone, which may have protective effects against hormone-related diseases such as breast cancer.

It is evident from our result that SO had remarkably lowered the percentage of abnormal sperm in VCR-treated mice compared with the corresponding mice treated only with VCR in all samples taken at different times after the end of treatment. Such percentages reached 4.72±0.20, 5.00±0.22 and 6.48±0.28 after treatment with the highest tested dose of SO at the three different exposure periods of spermatogenesis (1,3 and 5 weeks) respectively. A decrease in the slope of regression lines was observed between the dose of SO on VCR and the abnormal sperm after 1, 3 and 5 weeks from the treatment (Figure 4). Such decrease demonstrated insignificant negative correlation after 1 week from the end of treatment (r=0.129, P<0.646).

These results clearly indicated that SO efficiently prevents destruction of germ cells at different stages of development by inhibiting the generation of ROS generated during VCR catalysis. These observations are confirmed by the results of Hemalatha et al. (2004), who reported that the synergistic interaction of lignans and tocopherol in sesame oil reduces oxidative stress in animals fed sesame oil. According to Mishra & Acharya (2004), vitamin E prevents the degeneration of male germ cells by inhibiting lipid peroxides.

The probable mechanism of SO action include preventing the bioactivation of the mutagens (through inhibition of metabolic enzymes such as CYP450 family) (Lazarou et al., 2007), scavenging free radicals (Joshi et

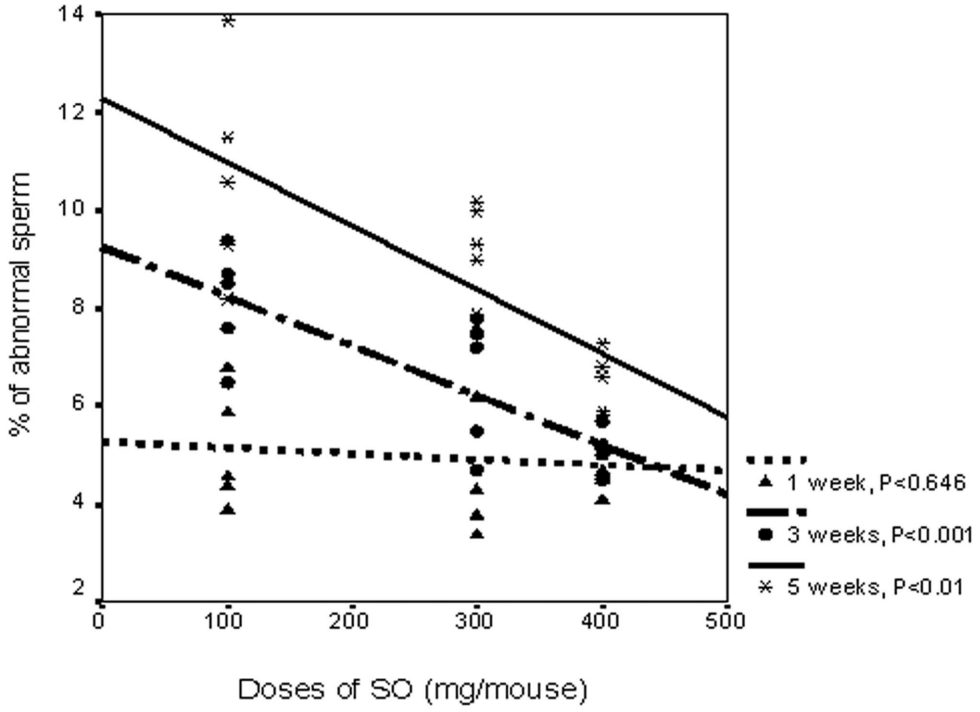

Figure 4. Linear regression analysis for the dose effect of SO on the percentage of abnormal sperm induced by VCR after 1,3 and 5 weeks treatment. Correlation coefficients of sperm abnormalities after 1, 3 and 5 weeks treatment (……) , (—— –), (——) were, respectively, r=0.129 (Y=5.285–0.001X), r=0.823 (Y=9.257–0.010X) and r=0.754 (Y=12.306–0.013X).

al., 2005), chelating metals ions (Hemalatha et al., 2004), modulating the antioxidant defense system (Satchithanandam et al., 1996) and may, therefore, protect the macromolecules like nucleic acids, proteins and lipids against oxidative damage and confer protection at cellular level (Parihar et al., 2006).

In conclusion, our work is an attempt of exploring the genotoxicity and antigenotoxicity of different doses of sesame extract. Taken together, these results indicated that the sesame extract was not genotoxic in somatic and germ cells but it contains components that exert antigenotoxicity effect on vincristine induced DNA lesion in mouse. Similarly, sesame extract was an effective antigenotoxic via its significantly inhibition of chromosomal aberrations in mouse bone marrow cells and spermatocytes and as for the induction of sperm abnormalities by vincristine.

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