Modulatory Role Of Pre- And Post- Treatment Of Spirulina Platensis On Mitomycin C Drug Induced Genotoxicity And Pathological Changes In Ehrlich Ascites Carcinoma Bearing Mature Female Swiss Albino Mice

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ABSTRACT
Mitomycin C (MMC) is a potent antitumor agent used against many cancers. It has a clastogenic and aneugenic effects. The protective effect of pre- and post- addition of Spirulina platensis (Sp) to the diet on MMC induced genotoxic effect and histopathological changes was evaluated in Ehrlich Ascites Carcinoma Cell (EAC) bearing mature female Swiss albino mice. The sixty EAC bearing female albino mice weighted 30-40 gm were observed along the experimental period and classified into six equal groups. The first kept as negative control fed on Sp powder free diet. the second kept as control positive fed on Sp powder 1% in their diet 3 weeks before tumor induction (Sp1), the third group fed on Sp powder 1% 3 weeks pre and one week post – tumor induction (Sp1+Sp2), while the fourth group intraperitoneally (i.p) injected with MMC (1mg/kg b.wt) on the third day post tumor induction and for 7 consecutive days, while the fifth group fed on Sp1 in diet for 24 days before MMC injection (Sp1+MMC) and the six group fed on Sp1 for 24 days pre- and 7 days post MMC injection (Sp1+MMC+Sp2) as the same previous dose and manner. The end of experimental period, 7 days from MMC injection, 3 animals from each group were sacrificed after 90 minutes from I.M injection of colchicine. MMC exhibited a significant increase in the frequency of micronucleated (MN) erythrocytes concomitant with several chromosomal aberrations and multiple histopathological changes in the bone marrow, liver and kidney. Pre- and post- treatment with Sp showed potent antclastogenic effect, regeneration of liver and kidney with restoration of bone marrow to the normal state. It can be concluded that Sp can minimize and mitigate the side effects of MMC on the normal cells and tissues of the body, so it can be pre- or post- treatment with MMC chemotherapy.

INTRODUCTION
Mitomycin C (MMC) is a powerful anti-bacterial and anti-tumour antibiotic isolated from Streptomycyes caespitosus. In cancer therapy, it is a commonly used drug to fight several human malignancies including cancers of the breast, bladder, cervix, colon, lung, pancreas, rectum, stomach and uterus. It is a direct-acting clastogen requiring only intracellular reductive activation to initiate its potent DNA cross-linking action (1). MMC appears to be toxic through oxidative stress mechanism (2). Intraperitoneal injection of 2mg/kg b.wt of MMC induced higher frequencies of micronucleus and chromosomal aberrations after 48 hours in bone marrow cells of mice (3). It induced various types of DNA damages that cause significant cytotoxicity to cells (4), although it was considered one of the most effective chemotherapeutic agents, but during clinical use several side effects may occur as genotoxicity in rat bone marrow cells (5) and renal toxicity (6). Moreover it is also carcinogenic (7), therefore strategies to protect against MMC induced genotoxicity and preserving the architecture of normal cells are of clinical interest.
Spirulina platensis (Sp) is a type of blue green algae that has been consumed for thousands of years as a primary food source as it contains high levels of antioxidants as carotenoids especially β-carotene (8), phycocyanin and phycocyanobilin (9). Moreover Sp significantly reduced both chromosomal damage and lipid peroxidation induced by cyclophosphamide and mitomycin C in mice (10). Sp exhibited anti-hepatotoxic (11) and anti-nephrotoxic (12) effects. Also several studies showed that Sp or its extracts prevent or inhibit cancer in humans (10). The aim of this study was to investigate a possible protective effect of pre- and post-treatment with Sp against genotoxic and pathological effects of MMC in EAC bearing female mice.

**MATERIAL AND METHODS**

Tested compounds

Mitomycin C (MMC) Kyowa. Co. Ltd (Tokyo-Japan), each vial contains Mitomycin C hydrochloride 10 mg potency, it was purchased from Eman-Elazab pharmacy, Zagazig City, Sharkia Proviance, Egypt.

Chemical formula (IUPAC):

Azirino -(2,3:3,4) pyrrolo,2-aindole-4,7-dione.6-amino-1,1a,2,8,8a,8b-hexahydro-18 (hydroxymethyl)-8amethoxy-5-methyl-carbamate.

Molecular formula: C_{15}H_{18}N_{2}O_{5}.

Spirulina platensis (Sp) is bright, blue-green powder. It was purchased from EL-Hellowa for Biological Products.

Experimental Design

Sixty adult female Swiss albino mice weighted 30-40 gm. were kept in metal cages under hygienic conditions, provided with food and water ad-libitum through the experiment. The animals were observed along the experimental period. Mice were i.p injection with 0.2ml portions of ascetic fluid containing 2.5×10^6 viable cells (EAC) (14), then divided into six groups of ten animals each. As shown in Table1.

![Fig.1. Chemical structure of MMC (13).](image)

At the end of the experimental period (7days post MMC injection), 3 animals of each group were sacrificed after 90 minutes of I/M injection of colchicine for chromosomal aberrations (17). The rest of animals were sacrificed and whole blood samples collected in EDTA containing tubes for micronucleus test (18). Femur bone, liver and kidney samples were preserved in 10% buffered neutral formalin for histopathological study and stained by Hematoxylin and Eosin (H&E) (19).

Statistical analysis was performed using one-way analysis of variance (ANOVA) procedure followed by Duncan's Multiple Range test (20). The 0.05 level of probability was used as the criterion for significance.

**RESULTS**

In the present study EAC bearing female Swiss albino mice characterized by increased size of abdomen with signs of emaciation and alopecia especially in MMC treated groups. After decapitation there was a large amount of ascetic fluid in the abdomen of mice due to EAC inoculation.
Table 1. Showing number of mice, line of feeding, induction of cancer, treatment and decapitation time

<table>
<thead>
<tr>
<th>Groups</th>
<th>No. of mice</th>
<th>Pretreatment with 1% Sp powder in food for 3 weeks before tumor induction*</th>
<th>Tumor induction</th>
<th>MMC (i.p injection of 1 mg/kg b.w) in 3rd day of cancer induction and for 7 consecutive days **</th>
<th>Post treatment with 1% Sp powder in food after MMC injection and for 7 days</th>
<th>Decapitation</th>
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<tbody>
<tr>
<td>Control</td>
<td></td>
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<td>+</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Sp1</td>
<td></td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Sp1+Sp2</td>
<td>Ten mice</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>MMC</td>
<td></td>
<td>-</td>
<td>+</td>
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<tr>
<td>SP1+MMC</td>
<td></td>
<td>+</td>
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<td>Sp1+MMC+Sp2</td>
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</tbody>
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* 1% of Sp powder mixed with normal food for 24 days from MMC injection (15)
** i.p injection of 1mg/kg b.w of MMC in third day of cancer induction and for 7 consecutive days (16).

Cytotoxic studies
Micronucleus test (MN)

There was a significant increase (p<0.05) of MN frequencies in erythrocytes of MMC treated EAC mice compared with control ones. This increase was significantly decreased in combined MMC and Sp treated groups (Figs. 2 and 3).

Chromosomal aberrations

MMC induced several chromosomal aberrations which were significantly high compared to control group (p<0.05). The aberrations include gap, ring, end to end association pulverization, hypoploidy and centromeric attenuation. Sp delivered a significant decline in chromosomal aberrations (Table 2 and Fig.4).

Fig.2. Effect of Spirulina platensis on MMC- induced micronucleus frequency in the erythrocytes blood smear of treated EAC bearing female mice (Means ± S.E.) (n=7).
Fig. 3. Photomicrograph of blood smear from EAC bearing female mice of different group showing: A. Sporadic micronucleated erythrocyte (Control) B. Sporadic micronucleated erythrocytes as control, (Sp1) C. Numerous micronucleated erythrocytes (MMC), D. Few micronucleated erythrocytes (Sp1+MMC+Sp2), (arrow, 1000x, Giemsa stain).

Table 1. Effect of administration of Sp (1% in diet) for 3 weeks prior to and one week concomitantly with MMC (1mg/kg b.wt) for consecutive 7 days on chromosomal aberrations in bone marrow of EAC bearing female mice (means ± S.E.)(n=3)

<table>
<thead>
<tr>
<th>Chromosomal aberrations</th>
<th>Groups</th>
<th>Control</th>
<th>Sp1</th>
<th>Sp1+Sp2</th>
<th>MMC</th>
<th>Sp1+MMC</th>
<th>Sp1+MMC+Sp2</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAC.</td>
<td>1.40±0.61&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.20±0.58&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.0±0.45&lt;sup&gt;c&lt;/sup&gt;</td>
<td>10.21±1.28&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6.01±1.14&lt;sup&gt;b&lt;/sup&gt;</td>
<td>6.20±0.73&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>CA.</td>
<td>2.01±1.27&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.61±0.75&lt;sup&gt;c&lt;/sup&gt;</td>
<td>2.01±0.89&lt;sup&gt;c&lt;/sup&gt;</td>
<td>8.01±0.89&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.41±0.75&lt;sup&gt;bc&lt;/sup&gt;</td>
<td>5.21±1.62&lt;sup&gt;ab&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>G.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1.61±0.75&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>1.21±0.8&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>2.01±0.89&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
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<tr>
<td>d.</td>
<td>2.01±1.26&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.61±0.98&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.21±0.80&lt;sup&gt;b&lt;/sup&gt;</td>
<td>6.01±0.63&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.20±1.02&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3.20±0.81&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
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<tr>
<td>EE.</td>
<td>1.61±0.98&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.61±1.17&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.01±0.89&lt;sup&gt;b&lt;/sup&gt;</td>
<td>7.61±0.75&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.01±1.26&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4.01±0.63&lt;sup&gt;b&lt;/sup&gt;</td>
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<tr>
<td>PULV.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2.01±1.10&lt;sup&gt;a&lt;/sup&gt;</td>
<td>-</td>
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<tr>
<td>R.</td>
<td>-</td>
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<td>-</td>
<td>2.01±0.63&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.21±0.49&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>1.21±0.81&lt;sup&gt;ab&lt;/sup&gt;</td>
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<tr>
<td>Hypo.</td>
<td>1.21±0.81&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>0.81±0.49&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.81±0.49&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>3.61±1.61&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>3.21±0.81&lt;sup&gt;ab&lt;/sup&gt;</td>
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<tr>
<td>TCA.</td>
<td>6.81±3.56&lt;sup&gt;c&lt;/sup&gt;</td>
<td>5.61±2.79&lt;sup&gt;c&lt;/sup&gt;</td>
<td>6.01±2.68&lt;sup&gt;c&lt;/sup&gt;</td>
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<td>18.01±1.67&lt;sup&gt;b&lt;/sup&gt;</td>
<td>18.80±1.02&lt;sup&gt;b&lt;/sup&gt;</td>
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Means with the same row carrying different superscripts are significantly at (P ≤0.05). TAC: total aberrated cells, CA: centromeric attenuation, G: gap, d: deletion, EE: end to end association, Pulv: pulverization, R: ring, Hypo: hypoploidy and TCA: total chromosomal aberrations.
Fig. 4. Photomicrograph of metaphase spread from bone marrow of EAC bearing adult female mice (2n=40) (1000x) (Giemsa stain) of; A. Control group showing normal metaphase chromosomes, B. Sp1 (1% in diet) for 3 weeks treated group showing normal metaphase chromosomes, C. MMC (1mg/kg b.wt.) treated group showing end to end association (EE), deletion (d) and ring (R), D. MMC (1mg/kg b.wt.) treated group showing centromeric attenuation (CA), E. MMC (1mg/kg b.wt.) treated group showing centromeric attenuation (CA) and gap (G), F. Sp1+MMC+Sp2 treated group showing deletion (d)

Histopathological findings

The bone marrow of control animals showed normal hematopoiesis with large number of megakaryocytes (Fig. 5,A), Sp1 treated group showed normal hematopoiesis with mild necrotic changes in the megakaryocytes (Fig. 5,B), while bone marrow in MMC (1mg/kg b.wt) treated group showed moderate depletion of bone marrow core (erythroid and lymphoid cells) with individual cell necrosis. The megakaryocytes were necrotic and rarely recorded (Fig. 5,C). On the other hand the bone marrow was restored to the normal erythroid and lymphoid cells besides normal megakaryocytes in Sp pre- and post-treated group (Fig. 5,D).

The liver of control groups revealed round cells aggregation in the portal area with normal hepatic architecture (Fig. 6,A) and just slight congestion, Sp1 treated group showed normal hepatocytes and sinusoidal architectures (Fig. 6,B) while MMC treated group showing intense aggregation of round cells and mild biliary hyperplasia (Fig. 6,C). On the contrary, the liver of Sp pre- and post-treated group with MMC showed normal liver with little hemorrhages and extramedullary hematopoiesis (Fig. 6,D)
Fig. 5. Photomicrograph from EAC female mice bone marrow of
(A) Control group showing normal hematopoiesis with large number of megakaryocytes (arrows), (Bar = 100 μm) (H&E).
(B) Sp1 group showing normal hematopoiesis (arrow) and mild necrotic changes in the megakaryocytes (arrow heads), (Bar = 100 μm) (H&E).
(C) MMC group (1mg/kg b.wt) for 7 days showing the disappearance of the megakaryocytes (arrow), interstitial edema and increase in the fat cells (arrow heads), (high magnification) (Bar = 100 μm) (H&E).
(D) Sp1+MMC+Sp2 group showing normal erythroid and lymphoid cells (arrow) with slightly decrease in the number of the megakaryocytes (arrow heads), (Bar = 100 μm) (H&E).
Fig. 6. Photomicrograph from liver EAC female mice of
(A) Control group showing round cells aggregation in the portal area (arrow) with normal hepatic architecture, (Bar = 100 μm) (H&E).
(B) Sp1 group showing normal hepatocytes and sinusoidal architectures, (Bar = 100 μm) (H&E).
(C) MMC group (1mg/kg b.wt) for 7 days showing portal area with intense aggregation of round cells (arrow) and mild biliary hyperplasia (arrow heads), (Bar = 100 μm) (H&E).
(D) Sp1+MMC+Sp2 group showing normal liver with little hemorrhages (arrow) and extramedullary hematopoiesis (arrow head), (Bar = 100 μm) (H&E).

Concerning the kidney, in control group showed normal with slight perivascular aggregation of round cells (Fig. 7,A) and also in Sp treated groups showed normal glomerular and tubular structures (Fig. 7,B) while kidney in MMC treated group showed glomeruli with shrunken glomerular tufts and dilated Bowman’s spaces besides vacuolation in renal epithelia (Fig. 7,C) controversially, kidney of Sp1 treated group before and concomitantly with MMC showed regenerative attempts in some renal tubule around slightly contracted glomerulus (Fig. 7,D).
DISCUSSION

MMC is a quinone-containing antibiotic; it has been used to treat a wide variety of tumors. Although current use of MMC is limited, this agent continues to be a key element in several clinical trials due to its intrinsic efficacy against many solid tumors and preferential activity in hypoxic tumoral cells. Metabolism of MMC may generate ROS, when ROS interact with cells and exceed endogenous antioxidant systems, there is indiscriminate damage to biological macromolecules such as nucleic acids, proteins and lipids (21).

Micronucleus (MN) assay and chromosomal aberration test were recommended by regulatory authorities for the assessment of genotoxicity and mutagenicity of many chemicals and natural compounds (5). MN was defined as a centric fragment of chromosome or a whole chromosome itself which lags behind in the cytoplasm during anaphase of cell division and does not get incorporated in the daughter nuclei (3). MN induction is a key characteristic of genotoxic compounds and analysis of micronuclei formation resulting from DNA strand breakage (clastogens) or interference with chromosome segregation (aneugens) (22).
The present study showed significant increase in micronucleated erythrocytes of the blood concomitant with several chromosome aberrations in bone marrow cells of MMC treated group in comparison with control groups and these results were consistent with (21) who recorded an increase in the number of MN at 24, 48, 72, and 96 hours post treatment of MMC. On similar ground MMC induced breakage mainly in the pericentromeric heterochromatin (22), 18 fold increase in MN, significant increase in hypoploidy and structural chromosome aberrations in metaphase preparations (23) and this finding was attributed to strong clastogenic effect of MMC (5). There was another explanation recorded by (24) who found that the treatment with MMC significant increase the occurrence of hypoploidy in the lymphocytes, a four-fold increase in kinetochore-positive MN in human fibroblasts. Which became in harmony with (25) who suggested that the increase in kinetochore-positive MN may related to the preferential binding of MMC to heterochromatin and induction of kinetochore detachment. All these previous findings have the potential to elicit aneugenic effects of MMC besides its strong clastogenic activity (26).

Controversially, the present study revealed that pre- or post-treatment with Sp had the same modulatory effect in both of micronucleated erythrocytes in blood and chromosome aberrations in bone marrow cells in comparison with MMC treated group which is in parallel to (2) who reported that pre-treatment with Sp significantly reduced micronucleated erythrocytes, chromosomal damage and lipid peroxidation induced by cyclophosphamide and mitomycin C in mice when applied to bone marrow cells. The previous findings fit in with the inhibitory effect of Sp on the in vivo chromosomal damage (2, 10) beside its anti clastogenic effect (27).

Regarding to the histopathological changes, there were several damages in the bone marrow and liver including disappearance of the megakaryocytes, interstitial edema and increase fat cells in bone marrow (Fig. 5, C) with intense aggregation of round cells and biliary hyperplasia in liver (Fig. 6, C) in MMC treated group in comparison with control groups, and this is due to MMC possess a quinone chemical structure which through a cascade of bioreductive process generates hydroxyl radical (OH-) which potentially can damage the DNA and other biomolecules of the cell. Since, free radicals (ROS) are highly reactive they can undergo reduction by oxidation of surrounding molecules (DNA, lipids, proteins) such damages to biological molecules by redox reactions may lead to numerous pathological disorders (28). obviously, bone marrow considered the prime target organ for MMC toxicity has some pathological changes after MMC treatment due to the metabolic activation of MMC to 2,7 diaminomitosene which cause bone marrow cytotoxicity, anemia, increase adipocytes, decrease RBCs and haemoglobin (29). The nephrotic effect of MMC as vacuolation in renal epithelia, shrunken glumerular tufts in (Fig. 7, C) nearly similar to that reported in study which found that MMC induced hemolytic uremic syndrome due to it can directly damage vascular endothelial cells of the kidneys (30).

On the contrary, treatment with Sp revealed the modulation in the pathological changes caused by MMC as it act as anti genotoxic (10), anti hepatotoxic (11) and anti nephrotic (12), this owed to Sp reputed to be an external source of the vital mitochondrial antioxidant enzymes as superoxide dismutase (31) which found to quench free radicals and prevents tissue damage (32). Sp exhibited protection and regeneration of liver cells and this in consistent with (33) who reported that oral administration of water extract of Sp for 7 days before cadmium toxicity reduced hepatic damage and this is due to the ability of Sp to scavenging free radicals by increasing level of antioxidant enzymes, as up regulation of ROS, hydroxyl groups, superoxides and hydrogen peroxides generations which in turn lead to oxidative damage to lipid contents of
membrane and induced liver toxicity. These characteristics can be attributed to the high levels of antioxidants such as vitamins, minerals, proteins, lipids, carbon hydrates, carotenoids and phycoerythrin in Sp. B-carotene decrease cell damage, especially the damage to DNA molecules, thus playing a role in the repair of the regeneration process of damaged liver cells (34). Phycoerythrin pigment significantly inhibited peroxyl radical induced lipid peroxidation in rat liver microsomes (35) Sp might be applicable to the reduction of general renal dysfunction, as Phycoerythrin constituent of Sp reduced the renal toxicity in rats caused by para-amino phenol (pain reliever), cisplatin (anti-cancer) (36), oxalate and mercury (32) as phycoerythrin reduced lipid peroxidation concomitant with restoration of renal function tests (37).

Acknowledgement

We thank Prof. Dr. Mohamed Hamed Mohamed, Professor of pathology, Faculty of Veterinary Medicine, Zagazig University for his help in carrying out histopathological study and Dr. Mohamed Abdo Ibrahim, Researcher, Animal Health Research Institute, Zagazig Lab for his help in carrying out cytogenetic study.

REFERENCES


المملوكت العربية

الدور التحديي لإضافة طحلب الإسبيرولينا القبلية والبعدي على التغيرات السمية الوراثية والمرضية لميتوسين

الميتوسينيسي في إناث الفئران البيضاء البالغة الحاملة للسرطان

مذبحة كفركي أبوالفتح، نبيلة إمام الشرقاوي، سماح رمضان السيد خليلى، منى محيى أحمد

قسم الطب الشرعي و السمووم – كلية الطب البيطري – جامعة الزقازيق

أجريت هذه الدراسة لتقديم تأثير إضافة طحلب الإسبيرولينا للعلاقة قبل وبعد حقن عقار
الميتوسينيسي في تخفيف التغيرات السمية الوراثية والمرضية الناتجة عن استخدامه في إناث الفئران
البيضاء البالغة الحاملة للسرطان. تم استخدام عدد ستون من إناث الفئران البيضاء الحاملة للسرطان (٢٠–
٣٠ جرام تقريباً) وتم متابعتها ورؤيتها خلال فترة التجربة وتقييمها إلى ست مجموعات متساوية. أُعتبرت
المجموعة الأولى كمجموعة ضابطة سابقة حيث تم تغذيتها بدون إضافة بوتادة طحلب الإسبيرولينا. أما
المجموعة الثانية أعطيت كمجموعة ضابطة موجبة حيث تم إضافة بوتادة طحلب الإسبيرولينا ١% في
العلاقة لمدة ٣ أسابيع قبل الحقن بالخلايا السرطانية. المجموعة الثالثة تم تغذيتها ب Inline-5 في
العلاقة لمدة ٣ أسابيع قبل و أسبوع بعد الحقن بالخلايا السرطانية. بينما تم حقن
المجموعة الرابعة بعقار الميتوسينيسي ١ مجم/كلم من وزن الجسم خلال السفارة البريتونية في اليوم الثالث
من حقن الخلايا السرطانية ولدمة ٢٤ يوم. أما المجموعه الخامسة تم تغذيتها على بوتادة طحلب الإسبيرولينا
لقد ٢٤ يوم قبل حقنها بالميتوسينيسي ١ مجم/كلم، ومن ثم مثل سائر المجموعات. والمجموعة السادسة فقما تم تغذيتها على
بوتادة طحلب الإسبيرولينا لمدة ٢٤ يوم و ٢٠ يوم بعد الحقن بالميتوسينيسي ١ مجم/كلم. ثم
تجمع عينات الدم لإجراء اختبارات كرات الدم الحمراء ذات الآلية المجهريه، وذلك بعد هذا التفاوت في
الكروموموسات في ٣ من الفئران التي سبق تغذيتها بالكوليستيروسين ٩٠ دقيقة قبل الذبح ثم اخذ عينات الدم،
لكد والكلى وحفظهم في الفريسالين المعتدل ١٠% لدراسة التغيرات الهيستوهيمولوجية.

لقد أظهرت النتائج عن أن معاملة الفئران بالميتوسينيسي أدت إلى زيادة معنوية في التغيرات الجينية
تشمل زيادة في عدد خلايا الدم الحمراء ذات الآلية المجهريه وزيادة في التغيرات العددية والتركيبية
للكرموسومات مع تغيرات بالتولوجية واضحة في نسجية النخاع. الكبد والكلى. بينما سجل استخدام طحلب
الإسبيرولينا تأثير معنوي في تخفيف التغيرات الجينية عن طريق تقليل عدد خلايا الدم الحمراء ذات الآلية
المجهريه وقليل التغيرات العددية والتركيبية في الكرموسومات سواء قبل أو بعد حقن الميتوسينيسي ١
مع عدم وجود فرق معنوي بينهما إلى جانب تقليل التغيرات بالتولوجية في نسجية النخاع، الكبد والكلى.

وقد خلصت هذه الدراسة إلى أن استخدام طحلب الإسبيرولينا سواء قبل أو بعد العلاج بعقار الميتوسينيسي
سي في الحيوانات الحاملة للخلايا السرطانية قادر على تقليل وتلطيف تأثيراته على الجينات والانسجة أثناء
المعالجة من السرطان. لذا نوصي باستخدام هذا الطحلب قبل أو قبل و بعد العلاج بالميتوسينيسي.