SUMMARY

Mitomycin C (MMC) is a highly active anticancer drug commonly used alone or in combination with other chemotherapeutic agents for the treatment of cancer of different types. Its bioactivities form critically damages the DNA present in both rapidly dividing cancerous cells as well as in normal cells.

Genotoxicity in the normal cells makes this drug highly toxic; thereby decreasing its therapeutic index for clinical use.

The present study investigated the chemoprotective potential of Oxyplex against MMC. Also it is an attempt to get some information about the possible danger of use Mitomycin-C as anticancer drug on chromosomes, sperm head of male mice and DNA damage. Also an attention has been focused on the protective effect of Oxyplex as antioxidant against MMC in male mice.

125 adult male mice ***Mus Musculus*** weighting approximately 20 gm and their ages approximately 7 weeks were used in this study.

The study included 5 groups;

Group 1: control negative group (-ve), composed of (5 males mice)

Group 2: control positive group (+ve), composed of (30 male mice). These animals were divided into 6 subgroups of

interperitoneal (I.P.) injection (6 hrs, 24 hrs, 48 hrs, 5 days, 2 weeks and 4 weeks. (Five males are used for each subgroup). And each mouse was given 0.0 4ml I.P. of 0.25% Mannitol in saline for each injection.

Group 3: (MMC): ***acute subgroups*** composed of (20 male mice). These animals were divided into 4 periods of interperitoneal injection (6 hrs, 24 hrs, 48 hrs, and 5 days), and each dose is 1/10 of LD50 I.P.

Chronic subgroups composed of (10 male mice). These animals were divided into 2 periods of interperitoneal injection 2 weeks and 4 weeks. (Five males are used for each subgroup), and each dose is 1/200 of LD50 I.P daily.

Group 4: 0xyplex group composed of (30 male mice). These animals were stored into 6 periods of interperitoneal injection (6 hrs, 24 hrs, 48 hrs, 5 days, 2 weeks and 4 weeks) (Five males are used for each subgroup). And each mouse was given 0.15 ml of solution daily (one capsule dissolved in 60ml of water. The dose used is 0.15ml daily for each mouse.).

Group 5: protective group composed of (30 male mice). In this group the animals injected by Oxyplex + MMC daily as the same in group 4.

All mice were subjected to the following:

1. Cytogenetic studies to observe the chromosomal aberrations and mitotic index.
2. Sperm head abnormalities were investigated.
3. Molecular studies which was detected by DNA fragmentation, laddering pattern, on gel electrophoresis.

The results showed that

1. Various chromosomal aberration including (structure and numerical aberrations) were observed in bone marrow cells of mice administrated by MMC treatment after all durations.

2. In comparison with the normal metaphase spread of control group, the encountered structure chromosome aberrations per 50 metaphase spread included by MMC treatment were deletions, fragmentations, centric fusion, break, centromeric attenuations, gaps, end to end associations and stickiness. All these types were significant difference in treated group as compared to the control one.

3. Meanwhile, the study revealed that MMC treated animals exhibited inhibition of mitotic activity as evidenced from the significantly lower level of mitotic index.

4. The treatment by MMC caused an increase in the sperm head abnormalities compared to the control such as amorphous, banana like, lack of hook and folded shape. Amorphous and banana like were the highest recorded of

aberrations at all durations and doses, while folded have the lowest.

5. Also, MMC induce DNA damage, appeared as fragmentation on gel electrophoresis.

As contrasted of the previous results the treatment of mice by Mannitol (control +ve) has no effects by comparison with the control animals.

On the other hand, Oxyplex has good effects on the animals treated by it.

6. Also, the animals treated by MMC + Oxyplex together become nearly as the control group at most durations of treatment. i.e. there is no significant difference between this group and the control –ve or control+ve groups.

7. ***So the protection effect was clearly observed*** in decreasing the number of deletions, fragmentations, centric fusion, break, centromeric attenuations, gaps, end to end associations and stickiness also the mitotic index increased. And decreasing the sperm head abnormalities and DNA damage.

Oxyplex at all durations dose has protective effects which were observed during co-treatment with MMC.

8. The present results indicate that Oxyplex is capable of suppressing all the aberrations induced by MMC in mice. Thus, Oxyplex may be a potent chemoprotective agent against the toxicity of the anticancer drug, Mitomycin-C.