Mitotic Gene Conversion and Monosomics Induced in Yeast by Cypermethrin and Calmepam

Dujana Yahya Al-Ayoubi
Girl's College of Education, Genetics, Riyadh, Saudia Arabia

ABSTRACT

The present investigation was planned to study the possible genotoxic effect induced by the insecticide cypermethrin and the drug calmepam upon yeast genome. In order to achieve such a purpose three yeast strains were employed. These strains are: 1-JD1 strain; 2-D7; and 3-D61-m strain. JD1 as well as D7 were used to investigate the convertogenic effect. D7 cells were used to study the effect of the tested chemicals upon mitotic crossing over. D61-m strain was used to study the clastogenic activity of the chemicals by measuring chromosome loss or induction of monosomics. The results obtained showed that the ten tested concentrations of both chemicals are toxic, since significant decreases in survivors were observed. The insecticide cypermethrin was proven to be a positive mutagenic agent upon the tested loci of D7 and JD1. The tested drug calmepam showed the same result. Cypermethrin and Calmepam were found to be positive clastogenic agents, since induction of significant increases in monosomics was achieved and a concentration-response relationship was observed.

INTRODUCTION

Synthetic Pyrethroids are a diverse class of more than 1000 powerful, broad spectrum insecticides used to control insect pests in agriculture, households, and stored products. Although they are based on the chemical structure and biological activity of Pyrthrum, an extract from plants in the genus Chrysanthenum, the development of synthetic pyrethroids has involved extensive chemical modifictions to make compounds that are more toxic and less rapidly degraded by light.

Pyrethroid toxicity is highly dependent on stereochemistry, the three dimensional configuration of the molecule. Each isomer (molecules consisting of the some atoms, but with different stereochemistry) has its own toxicity. Some pyrethroids have as many as eight different isomers and there are several different types. For example, many pyrethroids have pairs of isomers with different geometries, referred to as the cis and the trans isomers of Permethrin. The cis isomer is generally more toxic than the trans isomer (Ahmed 2002).

Acute toxicity of a mixture of two isomers depends on the ratio of the amounts of the two isomers in the formulation. For example, the female rate acute oral LD50 of Permethrin increases from 224 milligrams of the pyrethroid per kilogram of body weight (mg/ kg) to 6000 mg/ kg as the proportion of the trans isomer increases from 20 percent to 80 percent.

Most commercial formulations have a fixed isomeric ratio. Formulations made of a single isomer (Deltamethrin, for example) are likely to be much more toxic than those with four to eight isomers.

Route of exposure is critical in assessing the acute toxic potential of a pyrethroid. Based on laboratory tests with experimental animals, introduction of the compound into the brain is most toxic, followed by introduction into the blood vessels, introduction into the gut (intraperitoneal administration) oral exposure, inhalation, and dermal (skin) exposure.Introduction into the brain or blood vessels is more toxic than other routes of exposure as a result of the metabolic processes in mammals which rapidly detoxify the poisons and the slow rate of absorption by the gut, skin, and lung tissue.

Metabolites can also have an effect on the toxicity of a Pyrethroid. The mouse intraperitoneal LD50 of trans Resmethrin is greater than 1500 mg/ kg of body weight, it is over ten times less acutely toxic than three of its metabolites with LD50 that range from 46 to 98 mg/ kg. The common Pyrethroid metabolite Phenoxy benzoic acid may be significantly more toxic than the parent Pyrethroid. Deltamethrin, which is a primary metabolite of Tralomethrin has a higher acute toxicity than its parent compound.

In a number of separate mutagenicity studies (studies of the ability to cause genetic damage), cypermethrin allethrin, cismethrin, permethrin and fenpropathrin have shown some mutagenic effects.

Carcinogenicity studies of permethrin, resmethrin, fenvalerate and deltamethin have shown increases in various kinds of cancers. Only permethrin has been determined to be a potential or weak carcinogen by the U.S. Environmental Protection Agency. Carcinogenicity studies have also been done on phenothrin, allethrin and cypermethrin, none were carcinogenic.

A study of synthetic pyrethroids effects on persons engaged in packaging fenvalerate and deltamethrin in China documented burning sensations, tightness or numbness on the face, sniffles, and seneezes. Other symptoms included abnormal facial sensations, dizziness, fatigue, and skin rashes. In the five years (1983 – 1988) after pyrethroids began to be used in china, 573 cases (299 occupational and 344 accidental) of acute pyrethroid poisoning were reported of those, five resulted in death (Ahmed, 2002).

Calmepam is a paridylbenzodiazepine compound which has anxiolytic, mucle relaxant, sedative, hypnotic, anticonvulsant, and amnestic effects. It is used for several medical treatment such as management of alcohol withdrawal symptoms; control of muscle spasm, functional disturbances of the gastroint estinaltract; neurodermatitis and eczema... etc. When calmepam is used in conjunction with antiepileptic drugs, side effects and toxicity may be more evident.

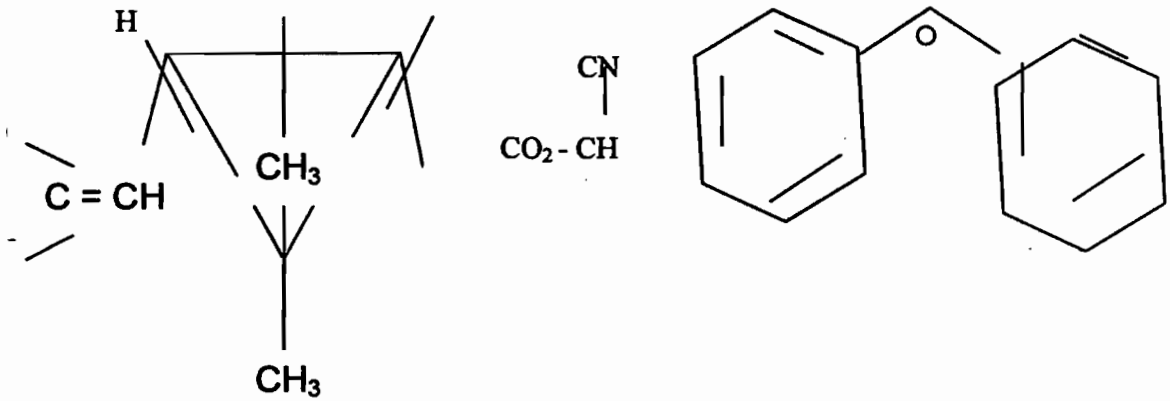
The present work was planned to investigate the capability of the insecticide Cypermethrin and the drug Calmepam in inducing mutagenic and clastogenic effect in yeast cells. In order to achieve such a purpose three strains of yeast

e employed. These strains are:1- D7 strain; 2 – JD1 strain; and D61-m in.

Mitotic gene conversion was assayed in D7 as well as JD1 strains; mitotic sing over was studied in D7 cells; and clastogenic activity or induction of osomics (chromosome loss) was examined in D61 m strain of yeast.

TERIALS AND METHODS

Three different strains of yeast were employed in this study. This work carried out at the Laboratory of Genetic Toxicology, Institute of Graduate es & Research, Alexandria University, in summer season of 2001. The mical structure of Cypermethrin is shown in Figure (1).



re 1. Chemical structure of the insecticide Cypermethrin

in D7

The diploid yeast strain D7 described by Zimmermann *et al* (1975) has been loped as a multipurpose system to detect a variety of biological genetic oints as follows :

i) Cellular toxicity, as measured by the inhibition of growth of cells on complete medium.

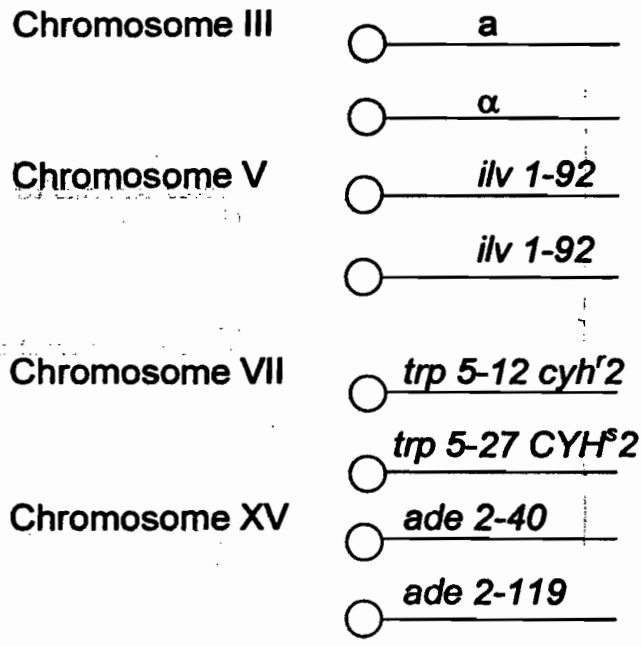
ii) The induction of nuclear point mutations at the isoleucine 1-92 allele, as measured by the production of isoleucine-independent prototrophs detected on isoleucine-deficient medium.

iii) The induction of cytoplasmic 'petite' mutations, as assayed by the production of the respiration-deficient colonies detected by their response to tetrazolium overlay medium.

iv) The induction of mitotic gene conversion at the tryptophan-5 locus as measured by the production of

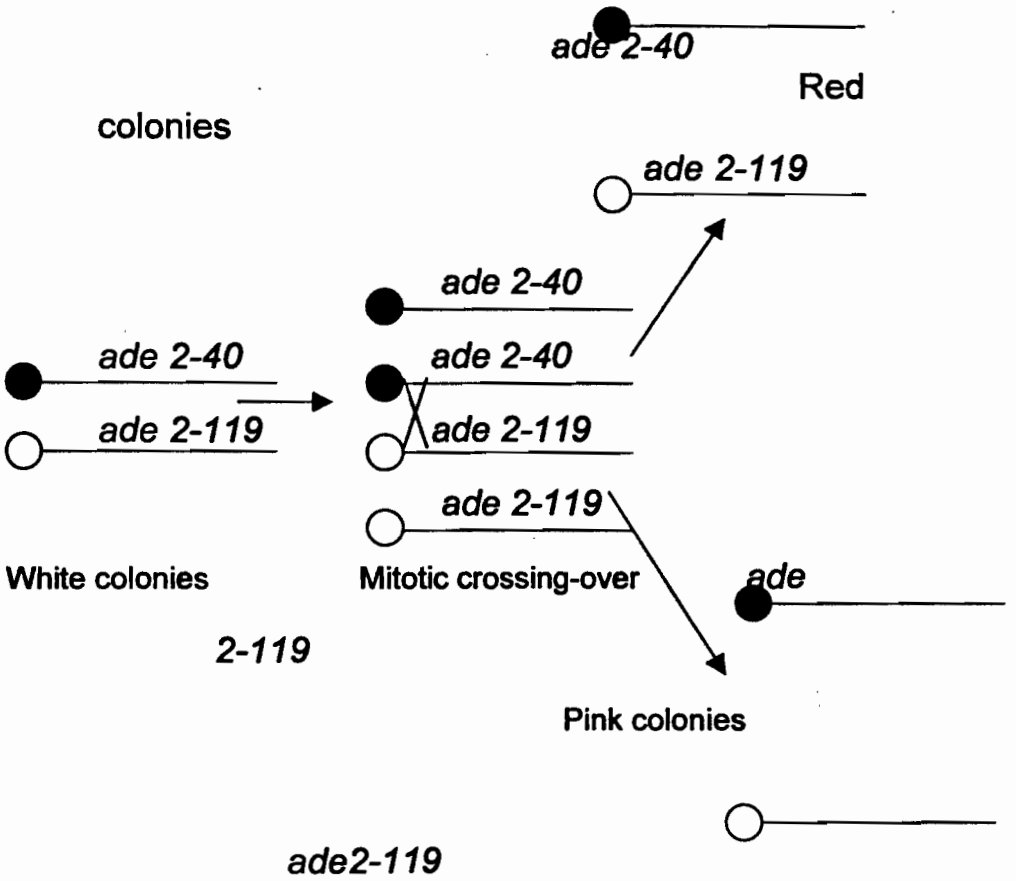
tryptophan-independent prototophs detected on tryptophan-deficient medium.

(v) The induction of mitotic crossing-over at the adenine-2 locus. The genotype of D7 is as follows :



Trp 5-12 and *trp 5-27* are heteroalleles of the TRP-5 locus and undergo mitotic gene conversion to produce prototrophic colonies carrying one wild-type allele which allows for growth on selective medium lacking tryptophan.

Ade 2-40 is a completely inactive allete of *ADE-2* which produces deep red coloured colonies, wherease ade 2-119 is a leaky allele accumulating only a small amount of pigment and thus producing pink colonies. In heteroallelic diploids the *ade 2-40* and *ade 2-119* alleles complement to give white adenine-independent colonies. Mitotic crossing-over can give rise to cells homoallelic for the *ade 2* mutations and so lead to the observation of red / pink half sectored colonies.



Mitotic crossing-over in D7 can also be measured using the recessive cycloheximide resistance allele *cyh*^{r}*2* on chromosome VII. Crossing-0ver between heterozygous *CYH2* and its centromere results in the production of colonies capable of growth on medium containing cycloheximide. Base-substitution mutation can be measured in D7 at the *ilv-1* gene by the production of isoleucine-independed colonies arising by reversion of the homo, zygous *ilv 1-92* alleles.

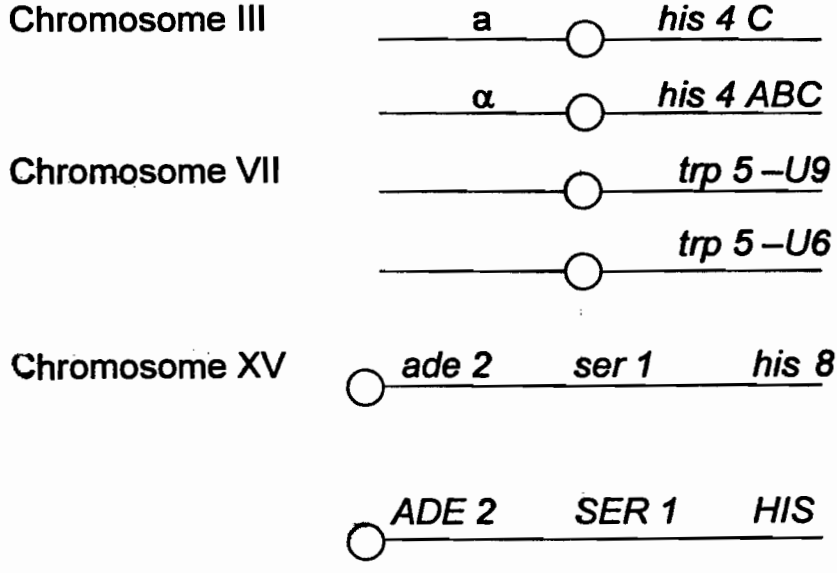
Gene Conversion

Gene conversion is assayed by the production of prototrophic revertants producted in a heteroallelic strain carrying two different defective alleles of the same gene. It can be distinguished from point mulation by the elevated levels of

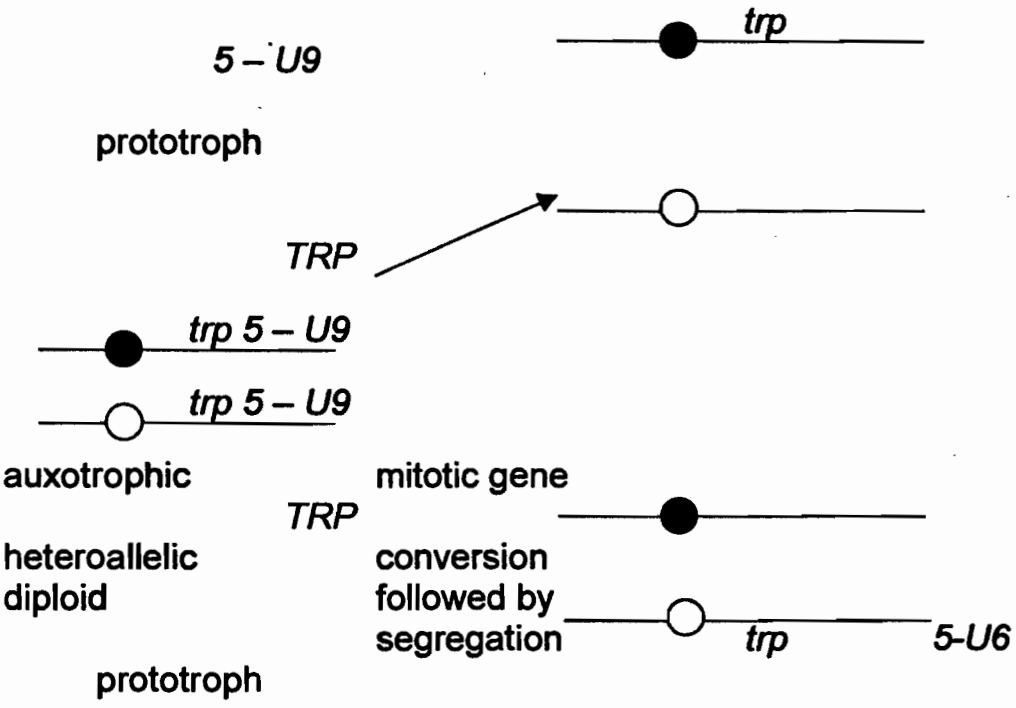
prototrophy produced in heteroallelic stains compared with homoallelic strains carrying two copies of the same mulation.

Strain JDI

As well as measuring gene conversion (Parry & Parry, 1984) , strain JDI is also capable of simultaneously detecting mitotic crossing-over on chromosome XV. The genotype of JDI is as follows:



his 4C, his 4ABC, trp 5-U9 and trp 5-U6 are heteroalleles at the His 4 and TRP5 loci, respectively. They undergo mitotic gene conversion to produce prototrophic colonies carrying one wild-type allele which allows for grows for growth on selective medium lacking either histidine or tryptohan, for example:



Yeast strain D61-m:

This strain is suitable for the induction and detection of chromosome loss (monosomy) in mitosis, chromosome gain (disomy) in meiosis, and diploidization in spores during meiotic division. D61m strain is described by Parry and Zimmermann (1976) and used to investigate the induction of chromosome loss (non-disjunction) occurring for chromosome VII. The genetic markers on this chromosome are:

Cyh2 + *leu* *ade6* *ade 2* *ilv* *1-92*

+ trp5

\+ + ade2 ilv 1-92

Since the chromosome loss unmasks the markers, leading to produce colonies that are white because ade6 sets a block the ade2 block and they require leucine and grow on media with cyclohexamide.

Methods:

Yeast strain D7:

Culture media

In the present study different media were used according to the genetic constitution of yeast strain.

Yeast extract peptone glucose broth (YEPG)

This medium was used for routine culture growth, consisting of 1% Difico yeast extract, 2% Difico bactopetptone supplemented with 2% glucose as a carbon source.

Yeast extract peptone glucose agar (YEPG agar)

This soild medium was used also for routine culture growth by adding 1.5% Difico agar-agar to YEPG.

D7 minimal growth medium

This medium was used for experimental treatments. It contains (per liter) : Diffico yeast nitrogen base without amino acids (6.7 gm), glucose (20 gm), and 60 mg of each of the following components; adenine sulphate, L-isoleucine and L-tryptophan.

Synthetic complete medium (SCM)

The medium was used in cell survival studies, and was composed of the following ingredients (per liter) : Difico yeast nitrogen base without amino acids (6.7gm), glucose (20 gm), adenine sulphate (5 mg), uracil (10 mg), L-arginine-HCl (10 gm), L-methionine (10 mg), L-tryptophan (10 mg), L-valine (30 mg) and Difico agar – agar (15 mg).

Selective medium (SM)

This medium was used for preparing selective agar plates to identify convertant colonies. It contained all components of the synthetic complete medium except tryptophan.

Preparation of cultures was carried out according to parry & parry (1984).

Yeast strain JD1:

The media used for JD1 strain were the same as those previously described for D7 strain except : 1) to minimal growth medium L-histidine (10 mg)

was added; and 2) selective medium lacking histidine was used. Drug treatment, scoring for convertants, and statistical analysis were the same as those for D7 strain.

Yeast strain D61-m:

Media for detecting monosomic colonies (YPEPG)

This medium was used as routine culture media. It was prepared as previously described in D7 strain media.

D61-m minimal growth medium

This medium was used for experimental treatments and contained (per liter) : Difico yeast nitrogen base without amino acids (6 gm), glucose (20 gm), adenine sulphate (10mg), L-isoleucine (30mg), L-tryptophan (10mg), L-leucine (30 mg), and L-histidine (10 mg).

YEPG agar:

This medim was used for preparing agar plates for cell survival studies, and its composition was described earlier.

YEPG agar + cyclohexamide:

This medium was prepared for identification of mutant colonies resistant to cyclohexamide. It was prepared by adding cyclohexamide (1.5 mg per liter) to the components of the yeast extract peptone agar medium.

Selective medium.

It was used to estimate the resistance of white colonies to cyclohexamide. It is composed of all components of synthetic complete medium except leucine.

Preparation of cultures and treatment were done according to description given by Parry & Parry (1984).

Statistical analysis:

Mitotic gene conversion and mitotic non-disjunction were subjected to linear regression analysis with the least square method according to the following equation. $Y = a + bx$

Where y is the mitotic gene conversion or mitotic non-disjunction induced frequency, and x is the concentration of the compound under study. The significance of coefficient of regression (b value) was tested using the analysis of variance (Snedecor, 1958 and De Bertoli *et al.*, 1980).

RESULTS

Cypermethrin

The effect of cypermethrin upon yeast genome is shown in Tables (1-4).

JD1 Strain:

The results obtained after treatment with cypermethrin are given in Table (1).

Survival percentages ranged from 100% for the control group to 16.81% after treatment with 50 µg / ml.

Convertants / 10^6 survivors were shown to be 2.6 for the control group. It ranged from 3.80 to 205.62 after treatment with 1 and 50 μg/mL, respectively. Statistical analysis showed that all tested concentrations (except one μg) were proven to decrease significantly the survival percentages of JD1 cells, reflecting a cellular toxicity of the tested synthetic pyrethroid cypermethrin. On the other hand analysis of variance indicated that all tested concentrations were positive in causing significant increases of convertants and a concentration-response relationship was achieved; giving an evidence that cypermethrin has convertogenic activiy upon JD1 genome.

D7 strain:

Table (2) illustrates the effect of the tested pesticide upon the survival percentages and convertants in D7 cells. The obtained results revealed that cypermethrin had capability to induce cellular toxicity for D7 cells. No survivors were obtained at the level of 50 μg/ mL. Induction of convertants showed that all tested concentrations were found to be positive in inducing significant increases in convertants; giving evidence that cypermethrin has convertogenic activity upon D7 strain.

Table (3) and Figure (4) show the effect of cypermethrin upon the induction of mitotic crossing over in D7 cells. All tested concentrations were proven to be positive in causing significant decreases in survival percentages and signifcant increases of mitotic crossing over; giving evidence that cypermethrin displayed mutagenic effect upon D7 cells.

D61 m strain:

Table (4) illustrates the cellular toxicity and clastogenic effect of cypermethrin upon D61 – m strain.

The higher concentrations 40 and 50 μg/ mL were proven to be completely toxic, since no survivors were observed. All tested concentrations were proven to be clastogenic, since significant increases of monosomics were obtained.

The results obtained from these experiments showed that cypermethrin is a positive mutagen and clastogen on yeast genome.

Calmepan:

JD1 strain:

Table (5) shows that 9 concentrations of this drug were found to be lethal, since significant decreases in survivors were achieved. Analysis of convertants showed that calmepam has convertogenic activity upon JD1 genome, since significant increases of convertants were obtained and a concentration- response relationship was observed (Table, 5 and Figure, 6).

D7 strain:

Table (6) shows the effect of the tested drug calmepam upon the convertants in D7 cells. The results obtained revealed that calmepam is a positive mutagen, since significant increases in convertants were obtained and a concentration-response relationship was observed. Such a result, was

confirmed from the analysis of mitotic crossing over (Table, 7 and Figure, 8). Calmepam wa proven to be a positive inducer of significant increases of mitotic crossing over. Ten-fold increases of mitotic crossing over were achieved.

D61- m strain:

Table (8) illustrates the effect of calmepam upon D61-m cells. The result obtained showed that calmepam, at the level of this study, is a positive clastogen, since significant increases of monosomics were obtained and a concentration-response relationship was achieved.

Table 1. Survival percentages and convertants of JD1 strain after treatment with cypermethrin

Concentration µg/ mL	X ± S. E. Survivors	X convertants/ 10^6 survivors
0	100.00 ± 0.00	2.6 ± 0.28
1	98.01 ± 2.1	3.80 ± 0.4
2	* 95.22 ± 2.2	* 8.40 ± 1.2
5	* 88.31 ± 3.1	* 20.30 ± 2.2
10	* 82.40 ± 4.1	* 30.20 ± 2.8
15	* 80.27 ± 4.2	* 40.40 ± 1.4
20	* 75.21 ± 2.2	* 56.50 ± 2.6
25	* 60.41 ± 3.2	* 80.20 ± 3.4
30	* 40.43 ± 2.3	* 97.11 ± 3.8
40	* 22.62 ± 4.1	* 20.42 ± 4.2
50	* 16.81 ± 3.2	* 205.62 ± 3.5

* : Significant at 0.05 level of probability.

Table 2. Survival percentages and convertants of D7 strain after treatment with cypermethrin

Concentration µg/ mL	X ± S. E. Survivors	X convertants/ 10^5 survivors
0	100.00 ± 0.00	1.64 ± 0.18
1	* 95 ± 1.2	* 4.4 ± 0.16
2	* 80 ± 2.3	* 8.6 ± 0.22
5	* 74 ± 2.4	* 20.3 ± 0.41
10	* 60 ± 3.2	* 30.8 ± 1.1
15	* 40 ± 2.8	* 50.4± 2.2
20	* 30 ± 4.2	* 55.2 ± 2.3
25	* 18 ± 3.7	* 60.6 ± 2.02
30	* 15 ± 2.4	* 65.8 ± 3.1
40	* 6 ± 2.2	* 68.4 ± 3.2
50	-	-

* : Significant at 0.05 level of probability.

Table 3. Survival percentages and mitotic crossing over after treatment of D7 strain with cypermethrin

Concentration ; µg/ mL	X ± S. E. Survivors	X Crossing over/ 10^5 survivors
0	100.00 ± 0.00	1.85 ± 0.048
1	* 96.1 ± 1.2	* 4.2 ± 0.2
2	* 90.2 ± 2.3	* 6.4 ± 0.2
5	* 80.2 ± 2.2	* 10.2 ± 0. 1
10	* 68.1 ± 2.4	* 12.7 ± 0.3
15	* 50.2 ± 3.2	* 14.6± 0.2
20	* 39.3 ± 2.6	* 18.8 ± 0.4
25	* 22.4 ± 2.2	* 20.2 ± 1.1
30	* 12.2 ± 3.4	* 24.3 ± 1.2
40	* 4.1 ± 2.1	* 32.6 ± 2.3
50	-	-

* : Significant at 0.05 level of probability.

Table 4. Survival percentages and monosomics of D61 m strain after treatment with cypermethrin.

Concentration ; µg/ mL	X ± S. E. Survivors	X Crossing over/ 10^5 survivors
0	100.00 ± 0.00	3.02 ± 0.21
1	* 97.2 ± 1.1	* 5.32 ± 1.1
2	* 95.1 ± 1.3	* 7.52 ± 1.2
5	* 84.3 ± 2.2	* 10.2 ± 1.3
10	* 82.2 ± 2.4	* 17.74 ± 2.2
15	* 70.4 ± 3.2	* 22.66 ± 4.1
20	60.5 ± 4.1	* 28.82 ± 5.2
25	* 42.2 ± 4.8	* 40.49 ± 6.1
30	* 28.5 ± 3.9	* 62.52 ± 6.4
40	-	-
50	-	-

* : Significant at 0.05 level of probability.

Table 5. Survival percentages and convertants of JD1 strain after treatment with cypermethrin.

Concentration ; µg/ mL	X ± S. E. Survivors	X Crossing over/ 10^5 survivors
0	100.00 ± 0.00	2.6 ± 0.28
1	* 98.3 ± 2.1	* 2.9 ± 0.10
2	* 97.4 ± 2.2	* 4.2 ± 0.10
5	* 95.2 ± 3.2	* 4.9 ± 0.30
10	* 92.5 ± 1.4	* 6.2 ± 0.22
15	* 90.4 ± 1.2	* 6.8 ± 0.30
20	* 88.1 ± 2.1	* 9.4 ± 0.41
25	* 84.2 ± 2.2	* 12.2 ± 0.60
30	* 80.1 ± 2.3	* 14.3 ± 0.82
40	* 60.5 + 4.1	* 22.8 + 1.2
50	* 38.4 + 2.5	* 32.3 + 1.4

* : Significant at 0.05 level of probability.

Table 6. Survival percentages and convertants of D7 strain after treatment with cypermethrin.

Concentration ; µg/ mL	X ± S. E. Survivors	X Crossing over/ 10^5 survivors
0	100.00 ± 0.00	1.64 ± 0.183
1	* 98.3 ± 2.1	* 1.82 ± 0.10
2	* 92.1 ± 3.4	* 4.2 ± 0.10
5	* 84.2 ± 2.1	* 5.74 ± 0.14
10	* 76.1 ± 1.8	* 7.33 ± 0.10
15	* 74.3 ± 1.6	* 12.14 ± 0.14
20	* 72.5 ± 2.4	* 20.32 ± 0.22
25	* 62.1 ± 3.1	* 28.40 ± 0.14
30	* 54.4 ± 2.8	* 42.11 ± 0.60
40	* 46.7 ± 1.4	* 53.20 ± 0.83
50	* 42.6 ± 2.2	* 59.14 ± 1.1

* : Significant at 0.05 level of probability.

Table 7. Survival percentages and mitotic crossing over after treatment of D7 strain with cypermethrin.

Concentration ; µg/ mL	X ± S. E. Survivors	X Crossing over/ 10^5 survivors
0	100.00 ± 0.00	1.85 ± 0.04
1	* 96.2 ± 2.2	2.21 ± 0.02
2	* 92.5 ± 2.11	* 4.38 ± 0.04
5	* 91.1 ± 2.10	4.89 ± 0.08
10	* 88.4 ± 2.17	* 6.22 ± 0.02
15	* 84.2 ± 1.20	* 10.30 ± 1.11
20	* 82.7 ± 2.3	* 12.42 ± 1.02
25	* 80.2 ± 4.1	* 14.22 ± 1.32
30	75.4 ± 3.6	* 15.33 ± 2.1
40	* 72.1 ± 1.38	* 18.60 ± 2.4
50	* 64.3 ± 2.32	* 20.22 ± 2.3

* : Significant at 0.05 level of probability.

Table 8. Survival percentages and monosomics of D61m strain after treatment with calmepam.

Concentration ; µg/ mL	X ± S. E. Survivors	X Crossing over/ 10^5 survivors
0	100.00 ± 0.00	3.02 ± 0.21
1	* 98.5 ± 1.20	* 5.32 ± 0.3
2	* 96.4 ± 2.40	* 7.44 ± 0.2
5	* 95.1 ± 2.02	* 7.69 ± 0.4
10	* 90.2 ± 3.20	* 9.22 ± 0.6
15	* 0.82.6 ± 2.8	* 11.30 ± 1.1
20	* 81.2 ± 2.2	* 12.02 ± 2.2
25	* 74.7 ± 2.6	* 18.11 ± 1.3
30	* 60.5 ± 3.4	* 22.40 ± 1.4
40	* 58.4 ± 4.5	* 40.32 ± 2.6
50	* 49.3 ± 3.8	* 46.22 ± 2.2

* : Significant at 0.05 level of probability.

DISCUSSION

Employing yeast (S. Cerevisiae) in genetics and genetic toxicology has been carried out by several workers (e.g. Hawthrone & Mortiner, 1960; Partrick *et al*, 1964; Zimmermann, 1968; Motimer & Manney, 1971; Parry, 1973; Byers *et. al.*, 1975; Schartz & Cantor, 1984; and Seehy *et. al.*, 1989 a&b).

Regarding the tested insecticide cypermethrin the induction of chromosomal aberrations and sister chromatid exchange in vivo in mouse spleen and bone marrow as well as in vitro in cultured mouse spleen cells by this insecticide was investigated (Amer *et al, 1987)*. The percentage of chromosomal aberrations in the spleen and in the bone marrow was almost the same and reached its maximum 6 h following i.P. injection. The aberrations induced were chromatid and chromosome gaps, fragments and tetraploidy. The insecticide caused a significant and dose-dependent increase in the frequency of sister chromatid exchanges (SCEs) in mouse bone-marraw cells; it reached 11.12 per cell and 4.4 for the control, respectively. The percentage of viable cells in mouse spleen cell cultures reached 87.4% and 99.9% relative to the control after treatment of the cell cultures with cypermethrin, respectively. All the tested concentrations of cypermethrin (0.25 – 400 µg/ ml) induced a high percentage of metaphases with chromosomal aberrations after 4 h of treatment. The mean frequency of SCEs per cell in spleen reached 15.1 $\pm$ 0.05 after treatment with cypermethrin at 4.00 µg/ml compared with 5.9 control. The results indicate that cypermethrin is genotoxic in mouse spleen and bone marrow, as well as in cultured mouse spleen cell. (Amer *et al.*, 1987).

Since the technical (chemically pure) grade of a Pyrethroid is usually formulated (mixed with carriers, solvents, etc.) for use in commercial pest control, the toxicity of these other ingredients must be taken into consideration when assessing the toxicity of formulated product. For example, Fenvalerate is much less toxic to mice than the formulated product, pydrin. A ten-fold difference in toxicity between formulations with the same active ingredient, but with different carriers, can be seen in some cases. Pyrethroid products formulated as emulsifiable concentrates (oil based formulations) usually have higher acute oral LD50 (are less toxic) in rats than wettable powder (aqueous) formulations (Ahmed 2002). Regarding the effect of cypermethrin, the results obtained showed that all tested concentrations were proven to be positive in inducing significant increases in convertants in JD1 as well as D7 cells. They also were found to be positive in causing chromosome loss in D61-m cells. These results, however, presents an evidence that cypermethrin is a mutagen and clastogen as well.

The genotoxic effect of the drug calmepam has now been investigated for the first time. The drug is shown to be a positive inducer of primary genetic damage, at the level of this study, and it is shown to be a positive clastogen at the level of yeast genome. However, further experiments, on mammals, are needed. The results obtained from this work are in agreement with those obtained by Miadokova *et al* (1992) and Amer *et al* (1987).

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الملخص العربي

التحول الچينى الميتوزى وأحاديات الكروموسوم المستحدثة فى الخميرة بالسيبرميترين والكالميبام

دجانه يحيى الأيوبى

كلية التربية للبنات – وراثة – الرياض – المملكة العربية السعودية

هدف البحث الحالى لدراسة الضرر الوراثى الذى يمكن أن يسببه المبيد الحشرى المسمى سيبرميثرين وعقار الكالميبام المستخدم فى عديد من الأغراض الطبية خاصة لكبار السن وذلك على خميرة الخباز.

تم اختيار ثلاث سلالات هى :

١- جـ د١ وهى تقيس التحول الچينى الميتوزى.

٢- د٧ وهى تقيس التحول الچينى الميتوزى والعبور الميتوزى.

٣- د ٦١ م وهى تقيس إنتاج أحاديات الكروموسوم.

تم اختيار عشر تركيزات من كل من المبيد والعقار قيد الدراسة وقياس:

١- السمية الخلوية.

٢- التحول الچينى الميتوزى فى موقعين مختلفين .

٣- العبور الميتوزى.

٤- أحاديات الكروموسوم.

وأظهـرت النـتائج المتحصل عليها قدرة هذه المركبين على إحداث سمية خلوية للثلاث سلالات الاختبارية الموظفة فى هذه الدراسة.

وأوضحت النتائج قدرة هذين المركبين على إنتاج تحول چينى ميتوزى مما يقلس قدريتهما الطفرية.

وبالنسـبة لأحاديـات الكروموسـوم فقد أظهرت النتائج وجود علاقة خطية بين التركيز المستخدم ومتوسط أحاديات الكروموسوم الناتجة مما يدل على قدرة المركبين – قيد الدراسة على تكسير المادة الوراثية.

ويدل هذا البحث على الأثر الضار وراثياً لمبيد السيبرميثرين وعقار الكالميبام.