[1]*IN VITRO* GENOTOXIC EFFECT OF TWO ORGANOPHOSPHORUS AND TWO PYRETHROID INSECTICIDES ON HUMAN LYMPHOCYTES

MOUSTAFA A. ABBASSY; A. H. BELAL; M. A. EL-SEEHY[1] AND A. H. MOSSA[2]

Dept. of Pest Control and Environmental Protection,
,Fac. Of Agriculture, Damanhour, Alexandria University, Egypt.

ABSTRACT

The widely used insecticides, chlorpyrifos, chlorpyrifos-methyl, cypermethrin and deltamethrin, were evaluated *in vitro* for their potential genotoxicity effect on peripheral blood lymphocytes of three groups of volunteers : smoker pesticide exposed volunteers (SPEV) ; non –smoker pesticide-exposed volunteers (NSPEV) and non-smoker non pesticide exposed volunteers (NSNPEV).Chromosomal aberrations (CA) were scored as genetic endpoint. Results revealed that the tested insecticides induced a significant increase in total chromosomal aberrations (CA) in pesticide exposed volunteer groups (SPEV and NSPEV) as compared with control groups in a concentration dependent manner. The highest genotoxic effect was obtained by chlopyriphos and the lowest genotoxic effect was obtained by chlorpyrifos-methyl. Overall results revealed that smoking and previously exposure of volunteers to pesticides increased chromosome aberrations of their lymphocyte cells.

Key words: human lymphocytes, smokers, volenteers, organophosphorus and pyrethroid insecticides , chromosomal aberration, genotoxic effect.

1-Dept. of Genetics, Fac. Of Agric., El-Shatby, Alex. Univ., Egypt.
2- Pesticide Chemistry Dept., National Research Centre, Dokki, Cairo, Egypt.

INTRODUCTION

Large amounts of pesticides are released daily into the environment and, hence, they represent a potential hazard not only to the human genetic material, but also to other living species, since their residues and derivatives are known to contaminante field crops. Several reports were demonstrated that many commonly used pesticides had genotoxic properties(IARC , 1991).

The organophosphorus (OP) and pyrethroid pesticides are known to possess high activity against abroad spectrum of insect pests and lack persistence in the environment (Vijveberg and Van den Bervken, 1990) . The impairment effects on public health of these pesticides cannot be denied. Genotoxic effects are considered among the most serious of the possible potential side effects of agriculture pesticides. Data of genotoxicity and carcinogenicity of OP and pyrethroid insecticides are rather controversial, depending on the genetic system or the assay used (Moretti et al., 1997). Therfore, this study aimed to further evaluate the potential genotoxic effects of sublethal doses of two OPs , chlorpyrifos & chlorpyrifos-methyl and two pyrethroids, cypermethrin & deltamethrin on humans lymphocytes.

MATERIALS AND METHODS

Test chemicals:

Two pyrethroid insecticides : Cypermethrin (25% EC), (RS) - α- cyano- 3- phenoxybenzyl (1RS, 3RS; 1RS, 3RS) - 3- (2, 2- dichlorovinyl)- 2,2- dimethyl cyclopropane carboxylate; and Deltamethrin (2.5% WP), (S) - α- cyano- 3- phenoxybenzyl (1R, 3R)- 3- (2, 2- dibromovinyl)- 2,2- dimethyl cyclopropane carboxylate.

Ttwo organophosphorus insecticides : Chlorpyrifos (48% EC), O, O- Diethyl- O- (3, 5, 6- trichloro- 2- pyridinyl) phoshorothioate and Chlorpyrifos-methyl (50% EC), O, O- Dimethyl- O- (3, 5, 6- trichloro- 2- pyridinyl) phoshorothioate. Also, standard carcinogenic compound: Benzidine (98% a.i.), 1, 1' - biphenyl- 4, 4'- diamine was used in this study.

Serial water dilutions for each compound were prepared and 100µl of each dilution were added to each culture as a concentrations equal to; (300µg a.i./ml and 120µg a.i./ml) from chlorpyrifos-methyl, (9.6µg a.i./ml and 3.84µg a.i./ml) from chlorpyrifos, (25µg a.i./ml and 10µg a.i./ml) from cypermethrin, (13.5µg a.i./ml and 5.4µg a.i./ml) from deltamethrin, and (30.9µg a.i./ml and 12.36µg a.i./ml) from benzidine as positive control and 100µl D.W. from negative control.

Sample collection:

Blood samples were collected from three different groups of volunteers (10 donors per group) of normal healthy male volunteers. The individuals of the 1st group were smoker pesticide-exposed volunteers (SPEV) . The individuals of the 2nd group were non-smoker pesticide-exposed volunteers (NSPEV) while the individuals of the 3rd group were non- smoker and non-pesticide exposed volunteers.

Cytogenetic methods:

The standard leucocytes cultures used in this investigation consisted of minimum essential medium (Eagle) with L-Glutamine (Sigma), supplemented with 10% fetal calf serum (Sigma) and 1% penicillin-streptomycin (1000 units 1000 µg/ml). For each 10 ml of this medium, 0.5 ml of whole blood, 0.25 ml phytohemaglutinin (Gibco) were added. The culture was incubated in tightly sealed tubes at 37ºC for 72 hrs. The proper concentrations of tested compounds (three replicate per concentrate) were added to the cultures 10 hrs. before harvesting. At 70 hrs. 20µl of colchicine, 10µg/ml (GIBCO), was added to each culture and the cultures were reincubated for 2 hours(Buckton and Evans, 1973). The culture was centrifuged for 8 min. at 1200 rpm, the supernatant was discarded and was suspended in a pre-warmed hypotonic solution (0.057 M KCl) for 10 min. at 30 ° C and centrifuged for 8 min. at 1200 rpm, then the cell pellet was fixative (methanol: glacial acetic acid, 3:1) for 20 min at room temperature. Samples for microscopic observation were obtained by carefully dropping cell suspension from a Pasteur pipette onto clean wet slides. They were air-dried, stained with 10% Giemsa (Goto *et al*., 1978). The cells were photographed and chromosomes were investigated for deletion, stickiness, exchange, fragment …etc.

RESULTS AND DISCUSSION

Cultures derived from human peripheral blood samples have been used for a number of years to detect chromosome aberrations. The preparations are used diagnostically in medical studies, to identify numerical changes and structural rearrangements in individual patients, and as a screening system for groups of workers exposed to potentially harmful agents (Garry, *et al*., 1990).

The *in vitro* effect of the tested insecticides on human lymphocytes revealed that these compounds caused significant increase in the total chromosome aberrations (CA) of the three different groups of human volunteers in a dose dependent manner . The highest increase in the percentage was observed in the first group (SPEV) and the lowest increase was found in the 3rd groups (NSNPEV), interaction-dependent manner as shown in tables (1 , 2 & 3) . The genotoxic effect of chlorpyrifos was more pronounced than that of chlorpyrifos methyl. .Also, chlorpyrifos was most toxic (acute oral LD_{50} for rats 135-163 mg/kg) than chlorpyrifos-methyl (acute oral LD_{50} for rats >3000 mg/kg) as recorded in Pesticide Manual (2003). The two OP insecticides contain the same structure except the substitution of ethyl groups in chlorpyrifos by methyl groups in chlorpyrifos-methyl which was less in its mammalian toxicity and genotoxicity than chlorpyrifos. This substitution may affect the intrinsic toxicity and genotoxicity and/or sensitivity of the structure to the metabolic systems in the treated rats. These genotoxic effects are in agreement with the findings of Lieberman *et al* (1998) that chlorpyrifos and diazinon have genotoxic effects even at domestically sprayed levels. Also tests using cells from human lymph nodes showed that chlorpyrifos causes an increase in the frequency of sister chromatid exchanges, SCEs, (Sobti *et al.*, 1982). A test using human white blood cells showed a similar increase in, SCEs (Nelson *et al.*, 1990). Chlorpyrifos caused genetic damage in human blood and lymph cells, mice spleen cells and hamster bone marrow cell (Cox, 1994). On the other hand, there is no available literature about the genotoxicity of chlorpyrifos-methyl.

Cypermethrin and deltamethrin are very active pyrethroid insecticides and are used to control pests of variety crops. Although

they considered to be safe for mammals (Perry *et al*., 1998), literature on *in vivo* genotoxicity of cypermethrin and deltamethrin are limited and rather controversial, depending on the genetic system or the assay used. Our results revealed that these insecticides caused significant increase in the percentages of total aberrations in blood lymphocytes of three different groups of human volunteers, (SPEV) , (NSPEV) and (NSNPEV) as shown in tables (1,2 & 3). Deltamethrin was more genotoxic than cypermethrin. It is well established that the two pyrethroids contain the same alcohol moiety (α-cyano-3-phenoxybenzyl), but substitution of 3(2, 2- dichlorvinyl)- 2, 2- dimethyl cyclopropane carboxylic acid in structure of cypermethrin by 3-(2, 2- dibromoviny) -2, 2- dimethyl cyclopropane carboxylic acid gives deltamethrin which was more genotoxic than cypermethrin. The above mentioned substitution may affect the intrinsic toxicity; genotoxicity and/or induced sensitivity of the structure to the metabolic systems in the treated rats (Abbassy et al , 2005).

These results in agreement and disagreement in some cases with those obtained by many authors. Surralles *et al.* (1995b), reported that cypermethrin has a weak genotoxic activity *in vitro*. In contrast, the same research group (Surralles *et al.*, 1995a) reported that cypermethrin did not increase the ratio of excision repairable DNA lesion converted to micronuclei. Nehez *et al.* (1998) reported that cypermethrin caused no significant increase in the chromosomal aberrations after rat treatments. Nehez *et al.* (2000) showed that treatment of rats with cypermethrin caused an increase in the number of aberration cells. Abdel Wahab (2002) reported that cypermethrin caused significant changes in mitotic activity of mice bone marrow cells. Also, data on the genotoxicity of deltamethrin are rather controversial, depending on the genetic system or the assay used (Villarini *et al.*, 1995). Beilschmidt, (1990) reported that fenvalerate and deltamethrin have shown increases in various kinds of cancers. The *in vitro* genotoxicity of deltamethrin has been evaluated by assessing the ability of the insecticide to damage DNA (as evaluated using the single-cell microgel-electrophoresis or comet assay) and micronuclei (MN) in human peripheral blood leucocytes (Villarini *et al.*, 1998). They found that in the presence of metabolic activation (+S9 mix), deltamethrin is able to induce DNA damage. The frequency of SCE and MN were not statistically increased in

deltamethrin-treated cells as compared to controls with and without S9 mix.

Finally, data in Table (4) summarizes the results of total chromosomal aberration percentages of human lymphocytes obtained from our study. It was noticed that control group in the first group of volunteers (SPEV) have the highest percentage of lymphocytes chromosomal aberration (12%) followed by the 2nd group (NSEP) (5%) and the 3rd group (NSNEP) (3%). Also, all formulated insecticides and reference carcinogenic compound increased total chromosomal aberration percentages of human leucocytes compared to control groups. The highest percentage of total aberration percentage was observed in first volunteers group (smokers and pesticide-exposed volunteers and the lowest was observed in third group of volunteers (non-smokers and non-exposed to pesticides).

The genetic effect of smoking (tobacco) and exposure to pesticides were described in studies using other test systems. An additive effect of smoking in inducing a chromosomal damage was also demonstrated, a significant increase in CA (Rupa *et al.,* 1988& 1989) and SCE (Padmavathi *et al.,* 2000 was observed in smokers compared with non-smokers from pesticide-exposed groups. A high frequency of chromosomal damage was detected in smoking greenhouse workers who had not used protective gloves (Lander *et al*., 2000).

In conclusion, our *in vitro* studies revealed that tested pesticides have definite genotoxic effect by using human lymphocyte cells. Smoking and previously exposure of volunteer persons to pesticides increased the aberrations of their lymphocyte cells. These findings support previous findings of Dulout *et al* (1985); Rupa *et al* (1989) and Scarpato *et al* (1996a, b).

The importance of study the genotoxic effects of pesticides is their association with increased cancer risk. Since, Hagmar *et al.* (1995) stated that an increase in the level of chromosome breakage appears to be relevant biomarker of future cancer risk.

Table (1): Effect of formulated insecticides and benzidine on chromosomal aberration in human lymphocytes of blood samples from smoker-pesticide exposed volunteers (SPEV).

Treatments	Concentration (µg a.i. /ml)	Chromosomal aberration (%)				[1]Total aberration(%)
		D	F	RCF	S	
Control	--	4	3	1	4	12
Chlorpyrifos-methyl	120	0	10	3	15	28*
	300	6	9	2	15	32*
Chlorpyrifos	3.84	0	11	0	23	33*
	9.6	12	15	6	19	52**
Cypermethrin	10	9	8	4	11	32*
	25	10	14	2	24	50**
Deltamethrin	5.4	10	11	0	13	34*
	13.5	19	18	9	24	70**
Benzidine	12.36	12	10	7	18	47**
	30.9	13	11	8	21	53**

[1]A number of 100 metaphases were counted; D: Deletion; F: Fragment; RCF: Robertsonian Centric Fusion; and S: Stickiness; statistical difference from the control: significant at P $\leq$0.05&**highly significant at P $\leq$0.01.

Table (2): Effect of formulated insecticides and benzidine on chromosomal aberration in human lymphocytes of blood samples from non-smoker pesticide-exposed volunteers (NSPEV).

Treatments	Concentration (µg a.i. /ml)	Chromosomal aberration (%)				[1]Total aberration(%)
		D	F	RCF	S	
Control	--	2	2	1	0	5
Chlorpyrifos-methyl	120	4	7	2	11	24*
	300	6	8	2	10	26*
Chlorpyrifos	3.84	4	7	2	15	28*
	9.6	12	13	4	18	45**
Cypermethrin	10	9	13	0	10	30*
	25	12	11	0	10	33*
Deltamethrin	5.4	11	10	0	10	31*
	13.5	9	14	0	13	36*
Benzidine	12.36	13	11	4	10	38*
	30.9	11	15	5	12	43**

[1]A number of 100 metaphases were counted; D: Deletion; F: Fragment; RCF: Robertsonian Centric Fusion; and S: Stickiness; statistical difference from the control significant at P $\leq$0.05&**highly significant at P $\leq$0.01.

Table (3): Effect of formulated insecticides and benzidine on chromosomal aberration in human lymphocytes of blood samples from non-smoker-pesticide non exposed volunteers (NSNPEV) .

Treatments	Concentration (μg a.i. /ml)	Chromosomal aberration (%)				[1]Total aberration(%)
		D	F	RCF	S	
Control	--	1	1	0	1	3
Chlorpyrifos-methyl	120	5	2	0	13	20*
	300	4	3	2	14	23*
Chlorpyrifos	3.84	3	8	2	10	23*
	9.6	13	10	0	12	35**
Cypermethrin	10	0	11	0	18	29*
	25	0	13	2	16	31*
Deltamethrin	5.4	10	8	0	12	30*
	13.5	10	9	1	12	32*
Benzidine	12.36	4	7	5	19	35**
	30.9	10	10	0	20	40**

[1]A number of 100 metaphases were counted; D: Deletion; F: Fragment; RCF: Robertsonian Centric Fusion; and S: Stickiness; statistical difference from the control significant at P ≤0.05&**highly significant at P ≤0.01.

Table (4): Effect of formulated insecticides and benzidine on chromosomal aberration in human lymphocytes of blood samples from different volunteers (SPEV) , (NSPEV) and (NSNPEV) .

Treatments	Concentration (μg a.i. /ml)	SPEV Total aberration (%)	NSPEV Total aberration (%)	NSNPEV Total aberration (%)
Control	--	12	5	3
Chlorpyrifos-methyl	120	28*	24*	20*
	300	32*	26*	23*
Chlorpyrifos	3.84	33*	28*	23*
	9.6	52**	45**	35**
Cypermethrin	10	32*	30*	29*
	25	50**	33*	31*
Deltamethrin	5.4	34*	31*	30*
	13.5	70**	36*	32*
Benzidine	12.36	47**	38*	35**
	30.9	53**	43**	40**

Statistical difference from the control significant at P≤0.05&**highly significant at P ≤0.01.

REFERENCES

Abbassy, M. A. ; A. H. Belal ; M. A. EL-Seehy and A. H. Mossa (2004) . *In vivo* genotoxic effects of two pyrethroid insecticides , cypermethrin and deltamethrin on male white albino rats. J. Agric. & Env. Sci. Alex. Univ., Egypt. Vol (3) , No. 2 : 27 – 38 .

Abbassy, M. A. ; A. H. Belal ; M. A. EL-Seehy and A. H. Mossa (2005) . *In vivo* genotoxic effects of two organophosphorus and one carbamate insecticides on white albino rats. J. Agric. Env. Sci. Alex. Univ., Egypt. Vol (4) No. 1 : 57 – 68.

Abed-El-Wahab, N. S. (2002). *In vivo* induction of and damage by insecticides, M. Sc. Thesis. Faculty of Agric. Daman. Alex. Univ. Dep. Of Genetics.

Beilschmidt, D. (1990). Toxicology and Environmental Fate of Synthetic Pyrethroids. Journal of pesticide Reform v.10,n.3.

Buckton, K. E. and H. J. Evans (1973) . Methods for the analysis of human chromosome aberrations. WHO, Geneva, pp 1-51.

Cox, C. (1994)."Chlorpyrifos, Part I-III: toxicology, human exposure, ecological effects". Journal of Pesticide Reform 14(4):15-20; 15(1): 14-20; 15(2):13-19.

Dulout, F. N.; M. C. Pastori and D. A. Olivero (1985). Sister-chromated exchanges and chromosomal aberration in apopulation exposed to pesticides. Mutat. Res., 143: 237-244.

Garry, V. F.; R. L. Nelson; J. Griffith, and M. Harinks. (1990). Preparation for human study of pesticide applications: Sister chromatid exchanges and chromosome aberrations in cultured human lymphocytes exposed to selected fumigants. J. Teratogenesis. Carcinogenesis and Mutagenesis., 10 (1) 21-29.

Goto, K. ; S.Maeda;Y. Kano;T. Sugiyama (1978). Factors involved in differential Giemsa-staining of sister chromatids. J.Chromosoma..,66(4):351-9.

Hagmar. L.; A. Brogger and I. L. Hansteen (1995). Cancer risk in humans predicted by increased levels of chromosomal aberrations in lymphocytes: Nordic study group on the health risk of chromosomal damage, Cancer Res., 54: 2919-2922.

IARC (1991). A Consensus Report of an IARC Monographs Working Group on the Use of Mechanisms of Carcinogenesis in Risk Identification (IARC intern. tech. Rep. No. 91/002), Lyon.

Lander, F.; L.E. Knudsen,; M.O. Gamborg; H. Jarventaus and H. Norppa (2000). Chromosome aberrations in pesticide-exposed greenhouse workers, Scand. J. Work. Environ. Health 26: 436–442.

Lieberman, A. D; M. R. Craven; H. A. Lewis and J. H. Nemenzo (1998). Genotoxicity from Doomestic use of organophosphate pesticides, Journal of Occupational and Environmental Medicine. 40: 954-957.

Moretti , M. R. Pasquini; M. Villarini ; G. Scassellati-Sforzolini and S. Monarca (1997) . Appicability of specific non-invasive methods for biomonitring of occupational exposure to deltamethrin ; preliminary study using an animal model. Arch. Environ. Contam. Toxicol. , 33 : 323-328.

Nehez, M.; R. Lorencz and I. Desi. (2000). Simultaneous action of Cypermethrin and tow environmental pollutant metals, cadmium and lead on bone marrow cell chromosomes of rats in sub chronic administration. Ecotoxicology and Environmental Safety. Section B 45(1):55-60.

Nelson, M. C.; Jalal, S. M. and Larson, O. R. (1990). Genotoxicity of the organophosphorus insecticide chlorpyrifos based on human lymphocyte culture. Cytologia, 55:589-592.

Padmavathi, P.; P. A. Prabhavathi and P. P. Reddy (2000). Frequencies of SCEs in peripheral blood lymphocytes of pesticide workers, Bull. Environ. Contam. Toxicol. 64: 155–160.

Perry, A. S.; I. Yamamoto; I. Ishaaya and R. Y. Perry (1998) Insecticides in Agriculture and Environment: Retrospects and Prospects. Springer-Verlag, Berlin, Germany.

Rupa, D. S.; P. P. Reddy and O. S. Reddi (1989). Frequencies of chromosomal aberrations in smokers exposed to pesticides in cotton fields, Mutat. Res. 22: 37–41.

Rupa, D. S.; P. Rita; P. P. Reddy and O. S. Reddi (1988). Screening of chromosomal aberrations and sister chromatid exchanges in peripheral lymphocytes of vegetable garden workers, Hum. Toxicol. 7: 333–336.

Scarpato, R.; L. Migliore. G. Angotzi; A. Fedi; L. Miligi and N. Loprieno (1996a). Cytogenetic monitoring of a group of Italian floriculturists : no evidence of DNA damage related to pesticide exposure. Mut. Res., 367: 73-82.

Scarpato, R.; L. Migliore; A. Hirvonen; G. Falck and H. Norppa. (1996b). Cytogenetic monitoring of occupational exposure to pesticides : Characterization of GSTM1, GSTT1 and NAT2 genotypes. Environ. Mol. Mut., 27: 263-269.

Sobti, R.C.; A. Krishan and C. D. Pfaffenberger (1982). Cytokinetic and Cytogenetic effects of some agricultural chemicals on human lymphoid cells in vitro: organophosphates. Mutat. Res. 102: 89-102.

Surralles, J.; N. Xamena; A. Creus and R. Marcos (1995a). The suitability of the micronucleus assay in human lymphocytes as a new biomarker of excision repair. Mutat. Res., 342: 43–59.

Surralles, J.; N. Xamena; A. Creus; J. Catalan; H. Norppa and R. Marcos (1995b). Induction of micronuclei by five pyrethroid insecticides in wholeblood and isolated human lymphocyte cultures. Mutat. Res., 341:169–184.

Villarini ,M.; M. Moretti and G. Scassellati-Sforzolini (1995) Studies on hepatic xenobiotic-metabolizing enzymes in rats treated with insecticide deltamethrin. J. Environ. Pathol. Toxicol. Oncol., 14:45-52.

Villarini, M.; M. Moretti; R. pasquini; S. Scassell; C. Fatigoni; M. Marcarelli; S. Monarca and A. Rodriguez (1998). *In vitro* genotoxic effects of the insecticide deltamethrin in human peripheral blood leukocytes: DNA damage (`comet` assay) in relation to the induction of sister-chromatid exchanges and micronuclei. J. Occup. Environ. Med., 40(1): 954-957.

Viveberg, H. P. M and J. Van den Bercken (1990) . Logical effect and the mode of action of insecticides Crit. Rev. Toxicol. 21 : 105 – 126 .

الملخص العربي

تأثير السمية الجينية (خارجيا *in vitro*) لاثنين من المبيدات الفوسفورية واثنين من المبيدات البيروثرويدية على ليمفوسيت دم الإنسان .

مصطفى عبد اللطيف عباسي – عبد السلام حلمي بلال[1] – عبد الباعث الصيحي[2] – عبد التواب حليم موسى[3]

1- قسم مكافحة الآفات كلية الزراعة بدمنهور
2- قسم الوراثة – كلية الزراعة – جامعة الإسكندرية
3- المركز القومي للبحوث الزراعية – الدقي - الجيزة

يهدف البحث إلى دراسة تأثيرات المبيدات الفوسفورية العضوية " كلوربيريفوس " ، " كلوربيريفوس ميثيل " ، المبيدات البيروثرويدية " سيبرمثرين " ، " دلتامثرين " خارجيا *in vitro* على الليمفوسيت lymphocytes من دم ثلاث مجموعات من المتطوعين : مدخنين ويتعرضوا للمبيدات نتيجة عملهم ، غير مدخنين ويتعرضوا للمبيدات ، غير مدخنين ولا يتعرضوا للمبيدات
وأوضحت النتائج ما يلي :

1. أن الشذوذات الجينية في حالة المقارنة في المجموعة الأولى (SPEV) كانت نسبتها مرتفعة (12%) عن المجموعة الثانية (NSPEV) (5 %) عن المجموعة الثالثة (NSNPEV) (3 %) .

2. كانت هناك زيادة معنوية في الشذوذات الكروموسومية الكلية في دم المتطوعين الذين يتعرضون للمبيدات وكانت الزيادة بصورة أكبر في حالة المدخنين الذين يتعرضون للمبيدات وكانت الزيادة بصورة أكبر في حالة المدخنين الذين يتعرضون للمبيدات .

3. كان مبيد الكلوربيريفوس أشد المبيدات في إحداث الشذوذات الكروموسومية بينما كان مبيد الكلوربيريفوس – ميثيل هو أقلها إحداثا لهذه الشذوذات .

4. التدخين يحدث ويزيد من حدوث الشذوذات الكروموسومية التي تحدثها المبيدات في خلايا الليمفوسيت الخاصة بدم المدخنين.