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Histopathological changes and metabolic gene polymorphism caused by aramite exposure in experimental rats

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Abstract

A total of 40 experiment rats (Rattus norvegicus) were divided into three groups of 10 rats for G.1 normal rats; 15 rat for G.2 that exposed to aramite with food daily for 90 days (5 g aramite/1 kg of pellet diet) and 15 rat for G.3 that exposed to aramite with water daily for 90 days(5 g aramite dissolved in 1 litter tap water). The result shows that the rats that were treated with aramite suffer from significant increased the activity and level of GPT; GOT ; ACP and ALP ($P \leq 0.05$) compared with control group , so the results fixed the histopathological changes in liver and intestine with clear mutation in *GSTM1* gene in rats that were exposed to aramite with diet and water compared with the normal control rats.

Key words : Aramite , *GSTM1, GSTT1*, Polymorphism.

Introduction

Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, and should be taken concerning cytogenetic and/or other/ tests that might become useful or mandatory[1]. Chemical carcinogens aramite has been used as an acaricide, such as in the control of mites in citrus fruits [2,3].However, its use has been discontinued and it currently has little commercial interest [4,5]. Although exposure through oral consumption of contaminated fruits is possible, it should no longer be occurring since the use of aramite as an acaricide has been discontinued[6,7].During the application of aramite as an acaricide occupational exposure is possible through dermal contact and inhalation of aerosols and dusts[8]. Aramite can be released directly into the environment through its use as an acaricide (miticide); however, this use has apparently been discontinued[9,10]. If released to soil, aramite is not expected to leach, If released to water, aramite may partition significantly from the water column to sediment and suspended material in water[11]. Based on no human data and sufficient data from animal bioassays including increased incidence of liver tumors and / or neoplastic nodules occure in three strains of male and female rats and males of one strain of mice, and extra hepatic biliary system tumors in dogs following chronic oral exposure [12,13] .The analytic laboratory of aramite from sample /of food/ with benzene, is concentrated & aramite is hydrolyzed with potassium hydroxide-isopropanol to form ethylene oxide. Evolved ethylene oxide is converted to formaldehyde with potassium iodide and formaldehyde is reacted with acetyl acetone to form colored compound which is determined calorimetrically [14] .In vivo metabolism studies in rats that were orally treated with a single dose of 200 mg/kg aramite and glycol ether were also found as primary metabolites in the excreta as well as in tissue samples; Following the analysis of the excreta and tissues ,only about 5% of the administered dose was accounted for as unchanged aramite or the primary metabolites, indicating that the primary metabolites are further degraded [15].The oral administration of a single close of 271 mg/kg benzene ring labeled 140 aramite to rats was followed by fast excretion of the radiocarbon ;Within 72 hours post dosage, 47% of the administered dose was eliminated via the urine. 32% via the faeces and the total carcass the

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contained approximately 90% of the administered radioactivity ;Identified metabolites excreted with the rat urine and faeces were tert-butylpyrocatechol and glycol ether [16,17].In cows treated with a single oral close of 4 mg / kg b.w. combined non-radioactive and 14C labeled aramite a similar excretion pattern was found; 54% of the administered dose was eliminated with the urine, 17% with the faeces and approximately 0.3% was found in the milk .In a feeding study, dairy cows were maintained on a diet containing 14C-labelled and unlabelled aramite at dosage levels of 3 and 20 ppm for 12 consecutive days; peak urinary excretion observed at the seventh test day reached values of 4 and 23 mg/kg respectively for the 3 and 20 ppm dietary level; peak faecal excretion was approximately 1 and 4 mg/kg and maximum milk residue values reached on the fourth test day were 0.02 and 0.06 mg/kg at the 3 and 20 ppm dose levels respectively. Residues in selected tissues ranged from 0.02 to about 1.3 mg/kg [18,19,20].Similar results were obtained after the daily administration of a diet containing 50 and 100 ppm aramite to lactating cows for a period of 27 days [18]Residues studies in hens that were treated with 3, 10 and 30 ppm 14C aramite in their diet for 30 days showed residue levels in eggs from 0.13, 0.49 and 0-145 µg/kg respectively at the 3, 10 and 30 ppm dose levels ; residues in muscle ranged from 2-12 µg/kg, liver 18-174 µg/kg kidney 2-25 µg/kg and fat 7-116 µg/kg depending on exposure level[21,22] .

Materials and methods

1- Animals:

A total of 40 male Rattus norvegicus rats weighing 200–250 g were used in this study. They were reared in the animal house of the science college .The animals were fed ad libitum with pellet diet and water.

2- Chemicals and reagent kits:

All chemicals and reagent kits that were used in this experiment were purchased from the traditional agriculture agency and health offices .

3- Experimental procedure:

In the experiment a total of 40 rats were used. The rats were divided into three groups of 10 rats for G.1 normal rats; 15 rat for G.2 that were exposed to aramite with food daily for 90 days (5 g aramite/1 kg of pellet diet) and 15 rat for G.3 that were exposed to aramite with water daily for 90 days (5 g aramite dissolved in 1 litter tap water). Each 30 days from the experiment period blood samples were collected from heart at volume 1ml from each rat for estimation of Glutamic oxaloacetic transaminase,Glutamic pyruvic transaminase [23].Acid phosphatase activity and alkaline phosphatase activity [24]. After 90 days, the animals were killed by decapitation; blood samples were collected for the purpose of genetics study; so liver , small and large intestine dissected out, washed with cold saline , and prepared for the purpose of histological study [25].

4-Genetic study:

1-Isolation of genomic DNA : Genomic DNA was isolated according to the procedure of [26].2-Multiplex PCR for GSTM1 and GSTT1 genotyping: the GSTM1 and GSTT1 genotypes were analyzed by multiplex PCR according to the protocol of [27]. Genomic DNA was amplified by using six sets of primers: GSTM1 Forward5'-GAA CTC CCT GAA AAG CTA AAG C – 3'and Reverse 5'– GTT GGG CTC AAA TAT ACG GTC G– 3', GSTT1 Forward 5'- TTC CTT ACT GGT CCT CAC ATCT C-3'and Reverse 5'– TCA CCG GAT CAT GGC CAG CA – 3' and Albumin Forward 5'– GCC CTC TGC TAA CAA GTC CTA C –3'and Reverse 5'-GCCCTA AAA AGA AAA TCG CCA ATC–3'. Albumin was used as control. The reaction mix include: green master mix 12.5µl , forward primer and reverse primer each 1µl , DNA 5µl, D.W. 1.5µl and mineral oil 25µl.PCR conditions were :I denaturation (1) 95 ^{o}C for 5 min. 1cycle,II denaturation (2) 94 ^{o}C for 1 min. ,III annealing 58 ^{o}C for 1 min. ,IV extension (1) 72 ^{o}C for 1 min. These steps 30 cycles and V extension (2) 72 ^{o}C for 5 min. 1cycle.

3-The PCR product was then subjected to electrophoresis on a 2% agarose gel. The presence of bands of 480 and 215 bps was indicative of the *GSTT1* and *GSTM1* genotypes; whereas the absence indicated the null genotypes for that gene. Albumin indicated by a 350 bp product was used as an internal control.

5-Statistical analysis :The data for various biochemical parameters were analyzed using Fisher exact and T-test [28].

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Results and Discussion

1-Glutamic Pyruvic Transaminase and Glutamic Oxaloacetic Transaminase :

Table (1 and 2) shows the activity of (GPT and GOT) in the blood of the normal and the experimental animals. There was a significant elevation in the activity of (GPT and GOT) enzymes during the exposure to aramite in diet and water compared with control group. Serum glutamic-pyruvic transaminase (GPT)and glutamic oxaloacetic transaminase (GOT)are enzymes which reversibly exchange amino and keto groups on alpha carbon positions of serum organic acids; these enzyme is prevalent in heart, liver, muscle and kidney tissue; its elevation in serum can be used for differential diagnosis involving these organs and indicate the integral stress[29].

Table(1)demonstrates the level of blood Glutamic pyruvic transaminase along experiment period IU

Groups	1 day before treatment with aramite	1st month post treatment with aramite	2nd month post treatment with aramite	3rd month post treatment with aramite
G.1	29.1±3.2 a	26.7±2.4 a	28.6±2.6 a	25.3±2.2 a
G.2	28.6±2.7 a	33.1±3.7 b	33.3±3.3 b	33.1±3.1 b
G.3	29.3±3.4 a	39.4±4.1 c	41.1±4.6 c	38.7±3.8c

*Values are mean ±standard error.**Vertical variable small letter refers to significant differences between groups at 5%.***LSD value=5.084 ..

Table (2) demonstrates the level of blood Glutamic oxaloacetic transaminase along experiment period/ IU

Groups	1 day before treatment with aramite	1st month post treatment with aramite	2nd month post treatment with aramite	3rd month post treatment with aramite
G.1	76.3±8.9 a	67.4± 6.7 a	61.2± 5.9 a	69.7±7.1 a
G.2	83.6±10.1 b	75.1± 8.2 b	75.7± 8.3 b	71.0± 8.3 a
G.3	86.1± 11.3b	85.7± 11.8c	86.7± 9.6 c	87.2± 8.9 b

*Values are mean ±standard error.**Vertical variable small letter refer to significant differences between groups at 5%.***LSD value=6.294.

2- Acid Phosphatase activity & Alkaline Phosphatase activity :

Table (3&4) shows the activity of (ACP) & (ALP) in the blood of the normal and the experimental animals. There was a significant elevation in activity of (ACP) enzyme during the exposure to aramite in diet and water compared with control group. Acid phosphatase(ACP) is a phosphatase, a type of enzyme, used to free attached phosphate groups from other molecules during digestion; it is stored in lysosomes and functions when these fuse with endosomes, which are acidified while they function; therefore, it has an acid pH optimum[30]. Alkaline phosphatase (ALP)is ahydrolase enzyme responsible for removing phosphate groups in the 5- and 3- positions from many types of molecules, including nucleotides, proteins, and alkaloids;the process of removing the phosphate group is called dephosphorylation [31]. Different forms of acid phosphatase and alkaline phosphatase are found in different organs, and their serum levels are used as a diagnostic for disease in the corresponding organs [32].Acid-/Alkaline Balance are a dualistic model representing the two opposite abnormalities of pH control ;the failure to maintain normal pH may be associated with one or more of seven causative factors such as water / electrolyte imbalance [33] . In fact excess alkalinity is just as harmful as excess acidity [34].

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Table (3) demonstrates the level of blood Acid phosphatase activity (ACP) along experiment period KAU/ dl

Groups	1 day before treatment with aramite	1st month post treatment with aramite	2nd month post treatment with aramite	3rd month post treatment with aramite
G.1	10.5± 1.3 a	11.3± 1.7 a	11.4± 1.6 a	10.3± 1.4 a
G.2	9.9 ± 0.9 a	16.1± 2.7 b	16.6± 2.7 b	15.3± 2.2 b
G.3	10.7± 1.6 a	22.3± 3.3 c	24.7± 2.3 c	21.9± 3.2 c

*Values are mean ±standard error. **Vertical variable small letter refers to significant differences between groups at 5%. **LSD value=4.113

Table (4) demonstrates the level of blood alkaline phosphatase activity (ALP) along experiment period KAU/ dl

Groups	1 day before treatment with aramite	1st month post treatment with aramite	2nd month post treatment with aramite	3rd month post treatment with aramite
G.1	32.3± 2.8 a	30.8± 2.6 a	27.9± 2.2 a	25.8± 2.1 a
G.2	32.3± 3.1 a	36.7± 3.4 b	34.6± 3.2 b	33.2± 3.1 b
G.3	30.9± 2.6 a	43.5± 4.5 c	46.1± 4.8 c	42.2± 4.3 c

* Values are mean ±standard error.**Vertical variable small letter refers to significant differences between groups at 5%.***LSD value=5.102.

The results in this study shows an increase in the levels of GPT , GOT, ALP and ACP in rats that were exposed to aramite which indicated that the liver is affected by harmful and toxic substance that was produced as free radicals from metabolite of aramite such as an increase in hydroxyl radical production; free radicals may also be formed via the auto-oxidation of unsaturated lipids in plasma and membrane lipids [35]The free radicals produced may react with polyunsaturated fatty acids in cell membranes leading to lipid peroxidation [36].The level of lipid peroxidation in cells is controlled by various cellular defense mechanisms consisting of enzymatic and non enzymatic scavenger systems [37].The levels of these defense mechanisms are altered and increased when exposed to toxic subastance therefore, the ineffective scavenging of the free radicals plays a crucial role in determining tissue injury[38], all these results are in agreement with [39] that fixed the role of aramite in producing harmful free radicals .

3- Histological changes :

a-Liver:

The most consistent feature of the hepatocyte in H&E stained sections is the basophilic stippling which corresponds to the rough endoplasmic reticulum (RER) (micrograph 1); these hepatocyte are found to contain ,glycogen, fat, store and metabolize vitamin A, and secrete type I collagen and detoxication function. The hepatocytes arranged to form the classic liver lobule is roughly hexagon-shaped with a central vein at its center and six portal triads at its periphery. A portal triad consists of hepatic arteriole; portal venule ;bile ductile and lymphatic vessel[40].The results that are obtained in this study fixed cardinal histological changes in liver of rats that is exposed to aramite compared with normal control group G1.The severity of these changes that is occurred in G3 group that exposed to aramite with water slightly more than G2 group that exposed to aramite with diet. These changes are demonstrated in glycogen degeneration fatty necrosis; mitotic figures in hepatocytes , proliferation of bile ducts and dilation of liver sinuses micrographs (2, 3, 4, and 5).Liver is the major organ that is affected with various diseases

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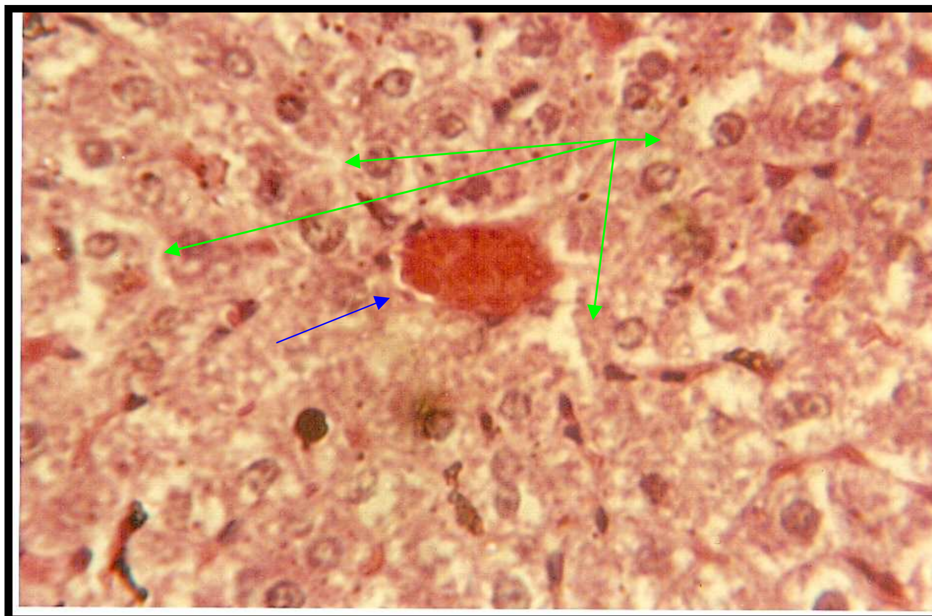
other than organs specially in the case of precence of toxic substances or its metabolite in the absorbent material. Degeneration is retrogressive changes in cells and tissues characterized by abnormal structural changes and decreased functions; it is nonspecific responses of cells and tissues following a variety of injuries. Some of these processes may be reversible if the injury is mild. If the injury is severe and persistent, it may progress to the point where the involved cell necrosis and cell dies[41].Glycogen degeneration involves the presence of abnormally large amount of glycogen in the cytoplasm of the cells. Glycogen is normally present in the cytoplasm of the cells(particularly in liver cells) . However, excessive accumulation occurs in some disease processes characterized by prolonged hyperglycemia such as diabetes mellitus or the presence of strong free radical ;also the reduction in food intake will quickly produce a loss of glycogen from hepatocytes and a reduction in RER [42].The microscopic changes are similar to acute cell swelling where clear vacuoles are present in the cells, because in routinely prepared sections, glycogen that is water-soluble is lost in the preparation[43].Necrosis is the name given to accidental death of cells and living tissue. In contrast with apoptosis,the cleanup of cell debris by phagocytes of the immune system is generally more difficult, as the disorderly death generally does not send cell signals which tell nearby phagocytes to engulf the dying cell. This lack of signaling makes it harder for the immune system to locate and recycle dead cells which have died through necrosis than if the cell had undergone apoptosis. The release of intracellular content after cellular membrane damage is the cause of the inflammation in necrosis[44].Severe damage to one essential system in the cell leads to secondary damage to other systems, so-called "cascade of effects". Necrosis is caused by special enzymes that are released by lysosomes which are capable of digesting cell components or the entire cell itself .The injuries received by the cell may compromise the lysosome membrane ,or may set off an unorganized chain reaction which causes the release in enzymes.Unlike in apoptosis,the cells that die by necrosis may release harmful chemicals that damage other cells[45].The other most common condition seen in the liver is the proliferation of bile ducts and dilation of the liver sinuses, The severity of these condition varies and may consist of only a few foci of proliferating ducts to large numbers of foci, which may become confluent and infiltration of the stroma by plasma cells and lymphocytes [46].This result agrees with many in vitro and in vivo metabolism studies in several animal species were confirmed the rapid degradation and hydrolysis of aramite to form free radical and the parent ester followed by other cleavage the formed products are polar alcoholic and phenolic compounds which can rapidly be excreted or further metabolized and incorporated into harmful chemical in natural tissue constituents by biochemical reactions [47].



Picture (1): Normal microscopic appearance of liver tissue (G1)shown central vein→ and normal arrangement of hepatocytes→ (E&H 285X).

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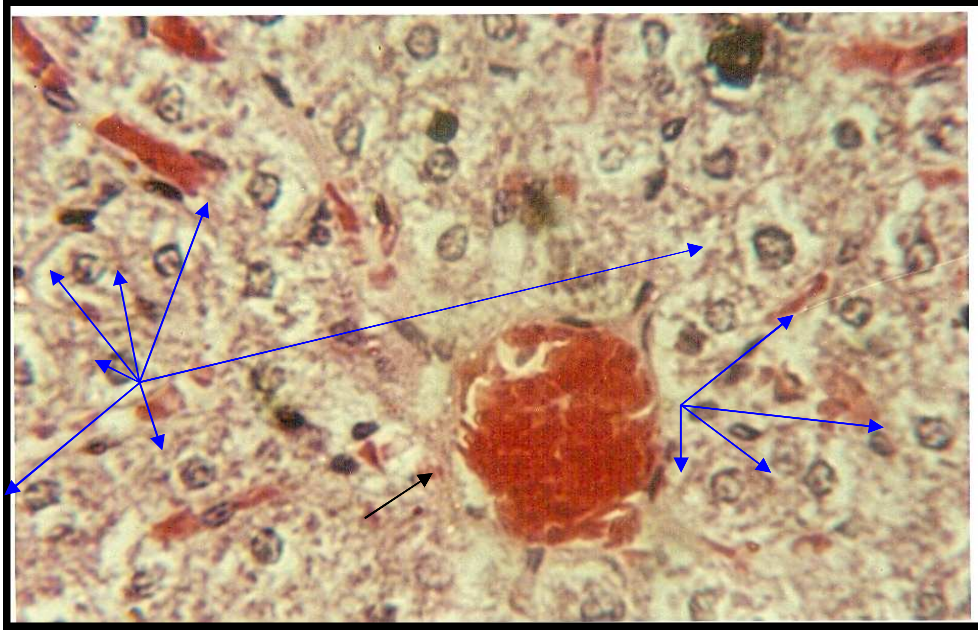
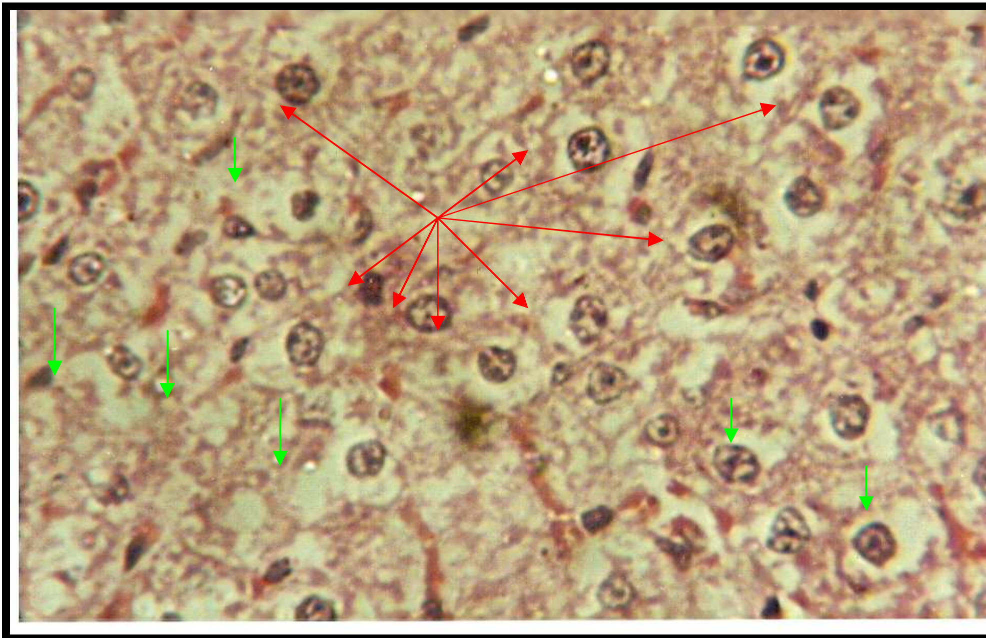


Picture (2): microscopic appearance of liver tissue (G2)shown dilation in central vein → with clear changes in hepatocytes arrangement and shape that appears as mitotic figures→ (E&H 285X).



Picture (3): microscopic appearance of liver tissue (G3)shown clear changes in hepatocytes arrangement and shape that appears as mitotic figures→ and clear cell change demonstrated by spaces in the cell cytoplasm where glycogen has been removed during histological processing → (E&H 285X).

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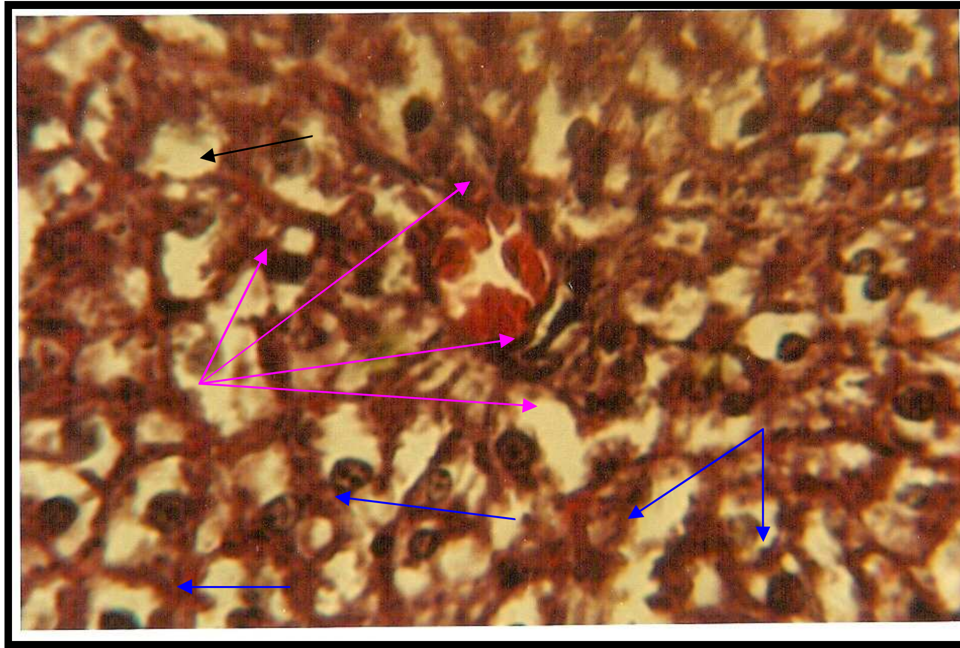
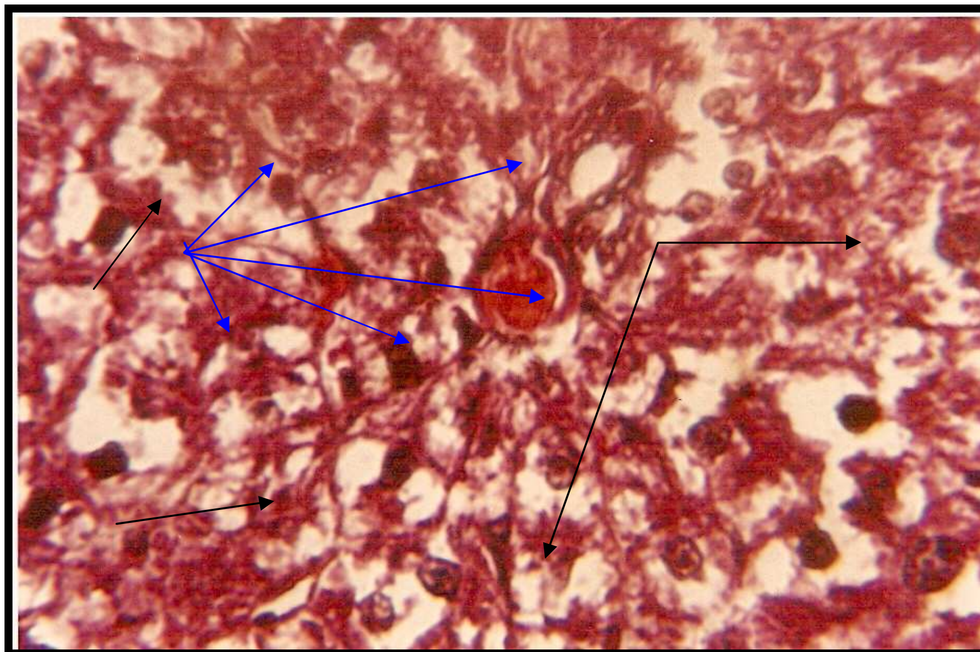


Picture (4): microscopic appearance of liver tissue (G2)shown large areas of necrosis as karyorrhexis and a few remaining viable cells around blood vessels→ with proliferation of bile ducts and dilation of liver sinuses → (E&H 285X).



Picture (5): microscopic appearance of liver tissue (G3)shown large areas of necrosis as karyorrhexis and karyolysis with a few remaining viable cells around blood vessels→ with proliferation of bile ducts and dilation of liver sinuses → (E&H 285X).

b-Small and large intestine:

General features of intestine : The small intestine is organized into a mucosa (consisting of an epithelium, glands, lamina propria, and muscularis mucosa), sub mucosa (connective tissue containing blood vessels, nerves, and Meissner plexus),

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muscularis (smooth muscle arranged as an inner circular layer and outer longitudinal layer and containing Auerbach plexus), and serosa. The inner luminal surface of the small intestine contains semi lunar ridges of mucosa and sub mucosa called plica circulars and is dotted with millions of openings, where the intestinal glands open to the surface, and finger like projections of the epithelium and lamina propria called villi (micrograph 6).The large Intestine is organized into the same layer that is present in small intestine with some modified in large intestine to suit its functions such as serosa contains fatty tags called appendices and the inner luminal surface is smooth (i.e. no rugae, plicae circulars, no villi) (micrograph 11). The results of histopathological examination that is done to know the effect of aramite as a harmful and a toxic substance fixed in the appearance of many changes; so there are construed as irregular arrangement of layer with tubular adenocarcinoma of ileum, fibrosarcoma ; accumulation of lymphocytes and Neutrophils forming a granuloma within the sub mucosa that may further extend into the muscularis externa; increased the thickness of irregular arrangement layer and hyperplasia of tubular glands; with demarcation between layers and present of the fibrohistiocytic sarcoma and lymphoma.(micrograph7,8,9,10,12,13,14 and 15).All the parts of intestine (small and large) are hypersensitive to certain external chemicals materials (specially denaturant protein).On the ingestion of these chemicals materials, a large number of lymphocytes, plasma cells, macrophages, and eosinophils accumulate within the lamina propria of the intestinal mucosa and result in the loss of normal arrangement of the layer and its consistency; these factors may contribute to the immunologic damage of the intestine[48].Cancer is a disease of the cells, which make up all the organs and tissues of the body, the cells are normally repaired and reproduce themselves in an orderly fashion; if for some reason this process gets out of control, a growth of tumour will ensue[49].The carcinogenic process was pictured as an orderly progression of the cell through three distinct stages: initiation by exposure to genotoxic agents; tumour promotion by agents that stimulate the initiated cell to proliferate and expand clonally to form a benign tumour, and progression in which the accumulation of the additional genetic damage in the expanding population of initiated cells cause the tumour to become malignant[50].

Carcinogens are now understood to be remarkably versatile, able to derail gene function by inducing mutations or by disrupting gene expression or both[51].So-called “non-genotoxic” agents, such as chlorinated organic compounds, hormones, and asbestos, are known to indirectly damage the genes via a number of different mechanisms,including alterations in gene the expression and oxidant formation[52].The current paradigm therefore, holds that cancer results from the accumulation of changes in the structure and expression of certain key genes by mechanisms as varied as point mutations induced by carcinogen-DNA binding, gene amplification, translocation, chromosomal loss, somatic recombination, gene conversion, or DNA methylation[53].At the center of the paradigm are the oncogenes and tumour suppressor genes that code for proteins serving as “relays” in the regulatory circuitry of the cell[54].Damage to these target genes can result in altered protein products or abnormal amounts of normal proteins, leading to deregulation of cell growth and differentiation[55].

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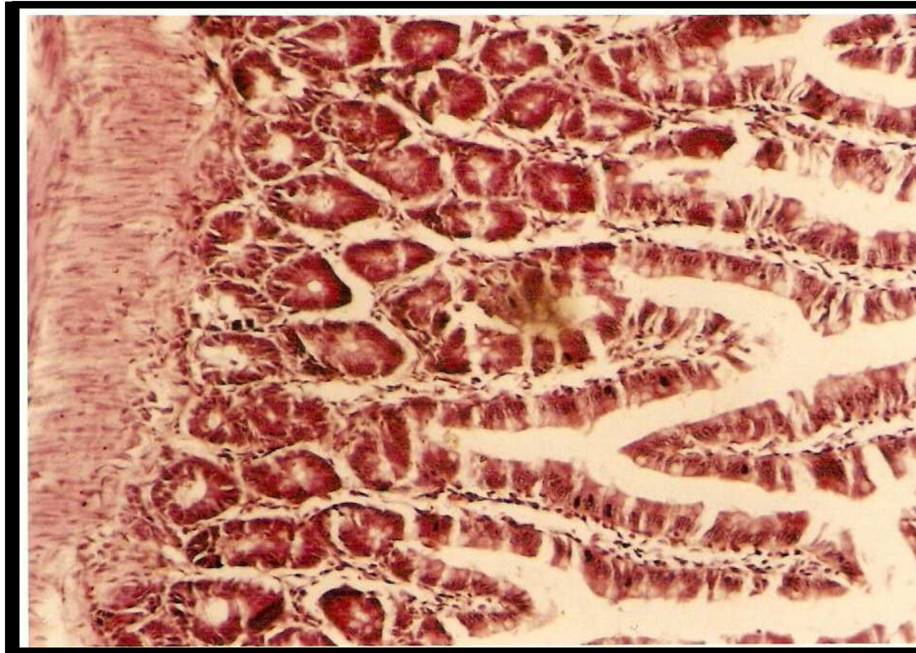
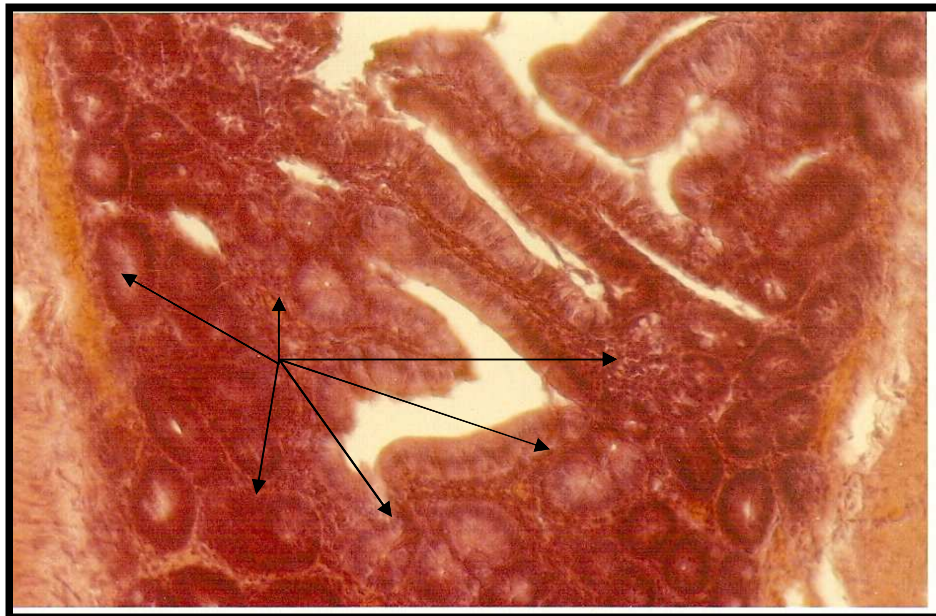


Picture (6): microscopic appearance of normal small intestine tissue-ileum (G1)shown the normal arrangement of layer and villi (E&H 250X).



Picture (7): microscopic appearance of small intestine tissue ileum (G2)shown irregular arrangement of layer with tubular adenocarcinoma of ileum→ (E&H 285X).

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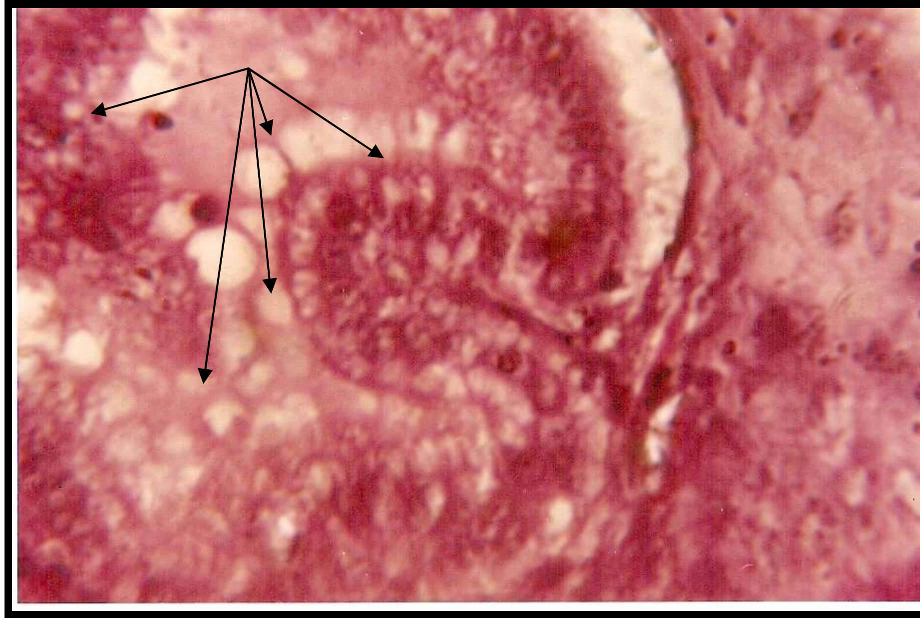
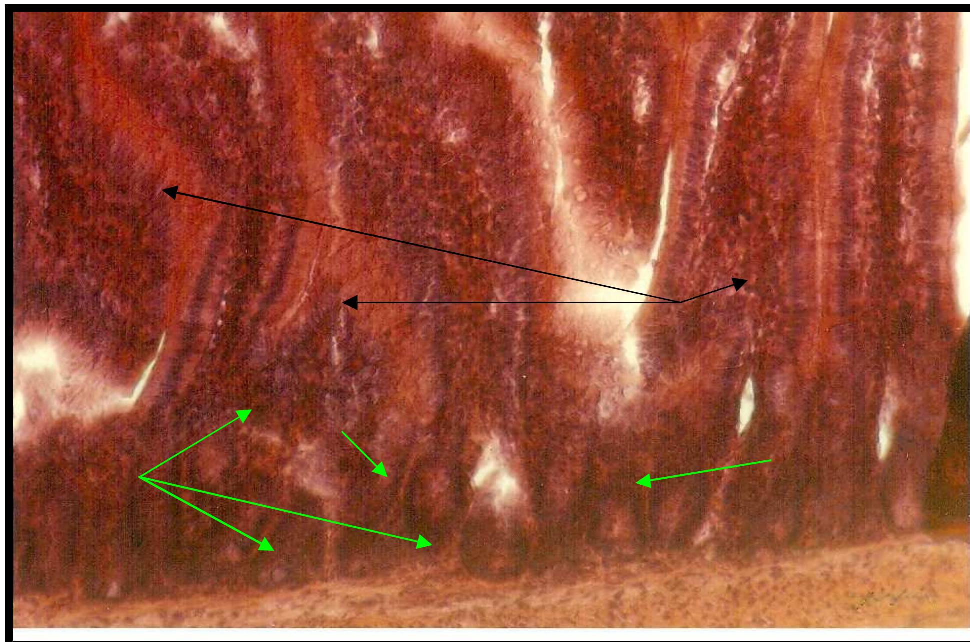


Picture (8): high power microscopic appearance of tubular adenocarcinoma of ileum in (G2) shown cells with intracellular accumulations of mucus to give the characteristic 'signet ring' appearance → (E&H 400X).



Picture (9): microscopic appearance of small intestine tissue ileum (G3)shown tubular adenocarcinoma of ileum→ with Fibrosarcoma→ (E&H 285X).

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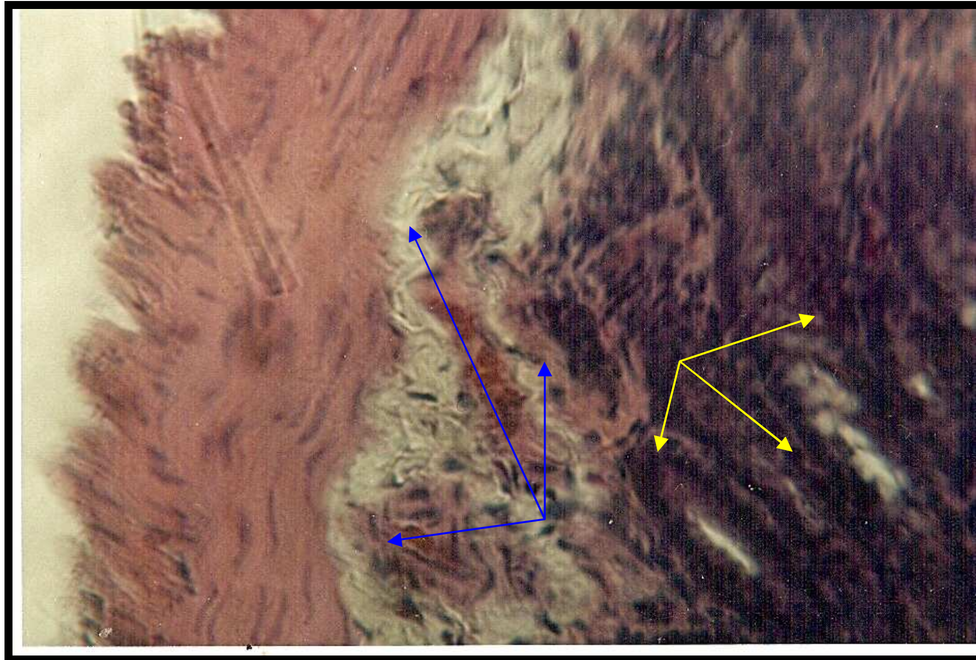
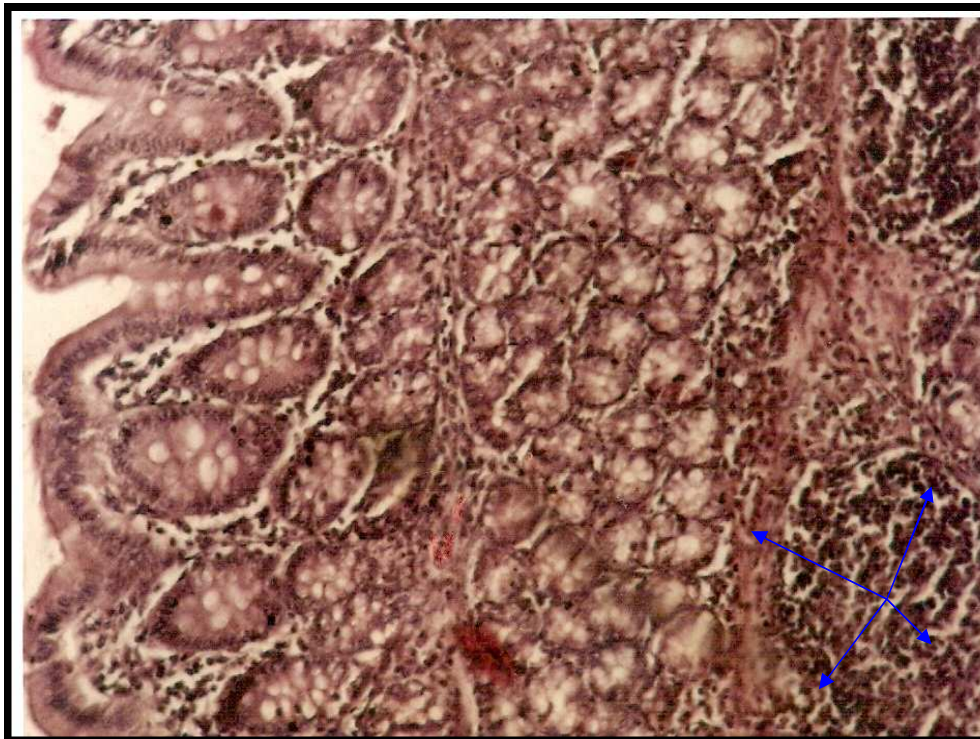


Picture (10):high power microscopic appearance of small intestine tissue ileum (G3)shown tubular adenocarcinoma of ileum→ with Fibrosarcoma→ with accumulation of lymphocytes and Neutrophils forming a granuloma within the sub mucosa that may further extend into the muscularis externa. (E&H 400X).



Picture (11): microscopic appearance of normal large intestine tissue-colon (G1)shown the normal arrangement of layer and normal size of lymph node→ (E&H 280X).

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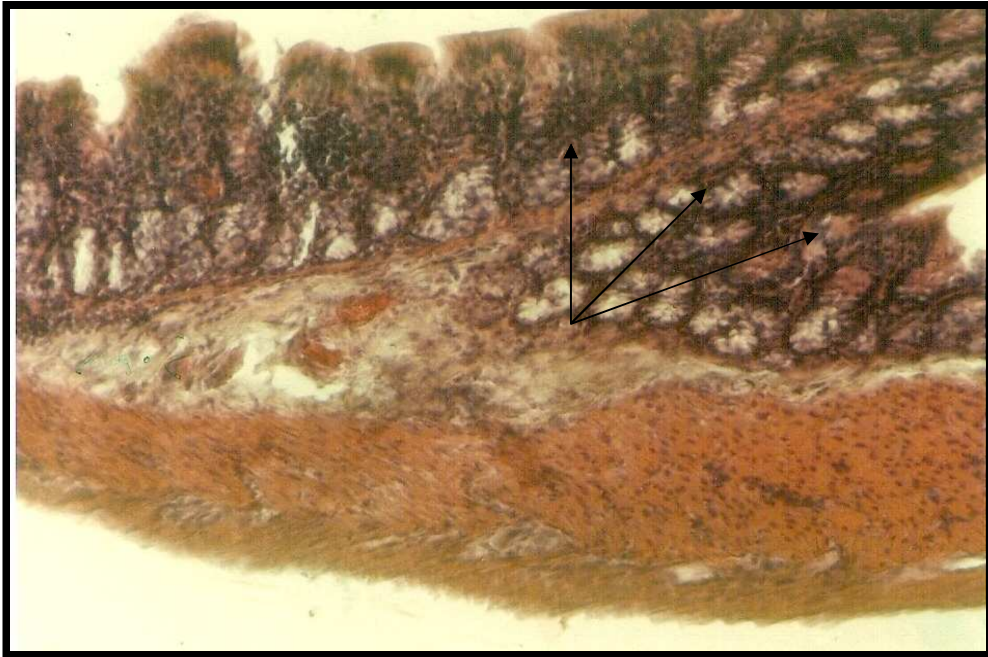
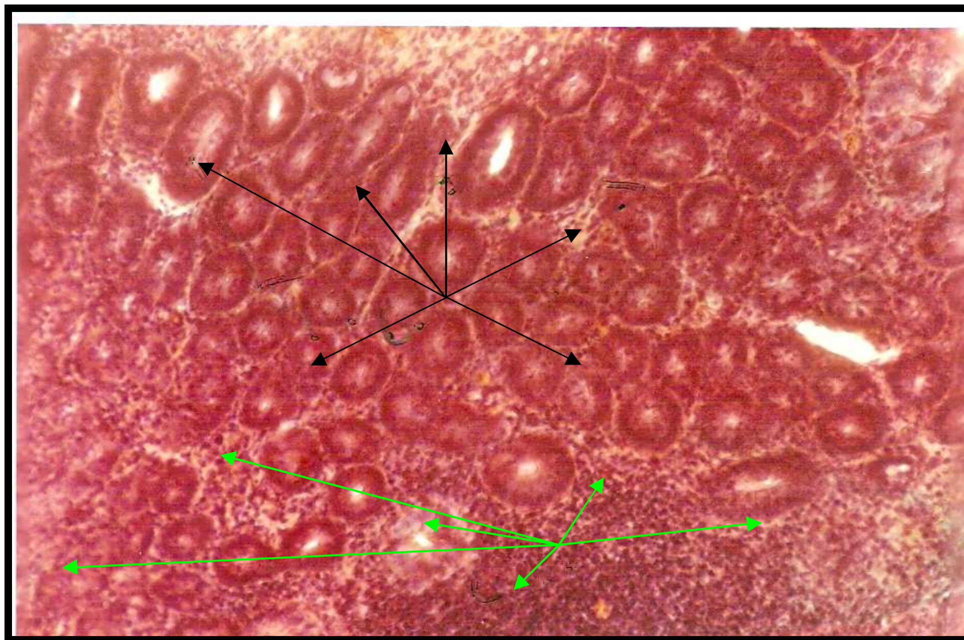


Picture (12): microscopic appearance of large intestine colon tissue (G2)shown increased the thickness of irregular arrangement layer and hyperplasia of tubular glands→ (E&H 285X).



Picture (13): microscopic appearance of large intestine colon tissue (G2)shown increased the irregular arrangement of hyperplasia of tubular glands→ with demarcation between layers and present of the fibrohistiocytic sarcoma and lymphoma → (E&H 285X).

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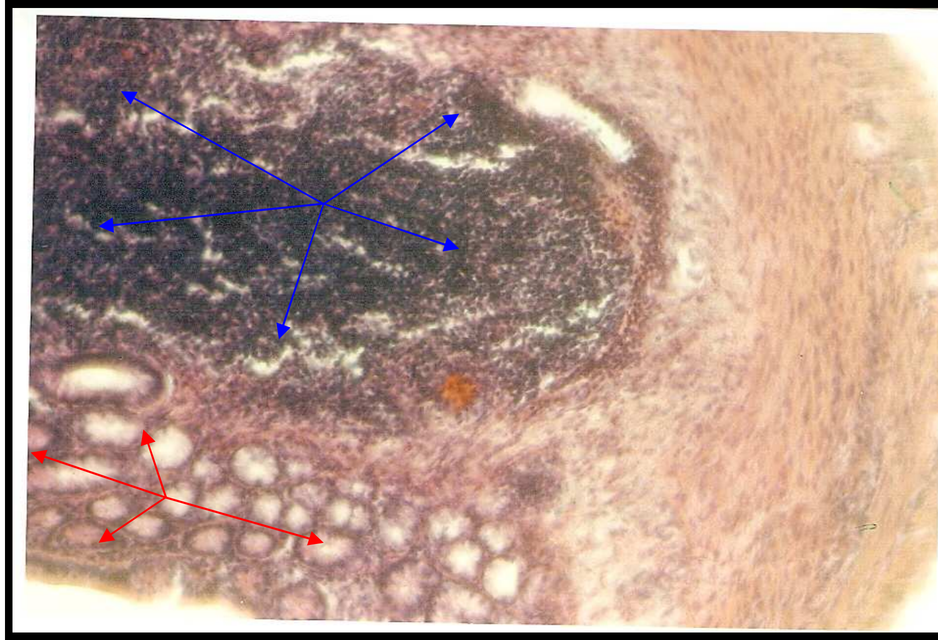
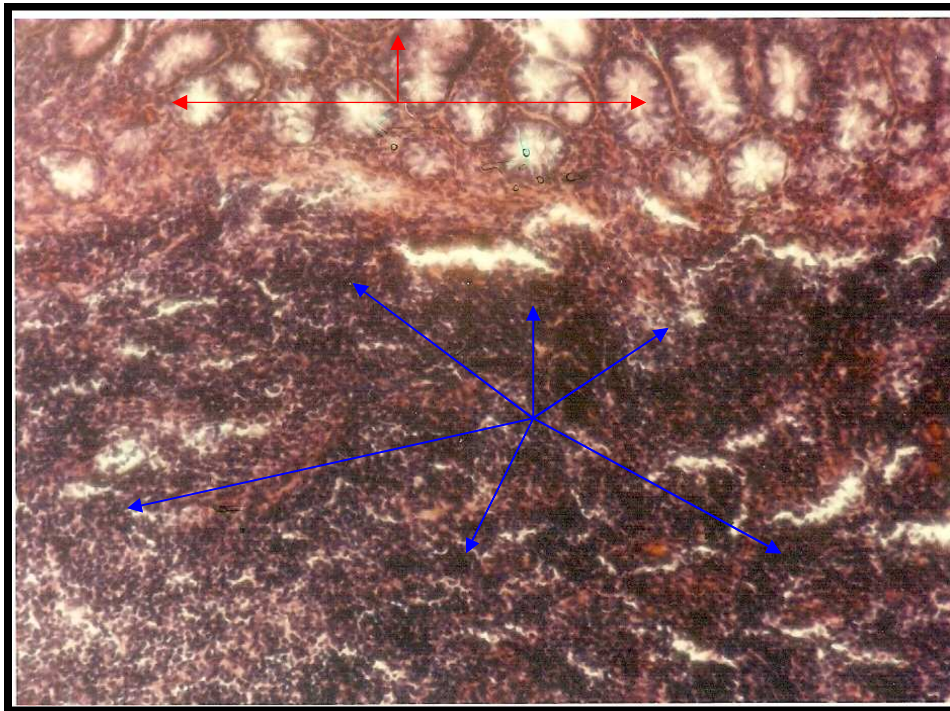


Picture (14): microscopic appearance of large intestine colon tissue (G3)shown increased the irregular arrangement of hyperplasia of tubular glands→ with demarcation between layers and present of the fibrohistiocytic sarcoma and lymphoma → (E&H 285X).



Picture (15): microscopic appearance of large intestine colon tissue (G3)shown increased the irregular arrangement of hyperplasia of tubular glands→ with demarcation between layers and present of the fibrohistiocytic sarcoma and lymphoma → (E&H 285X).

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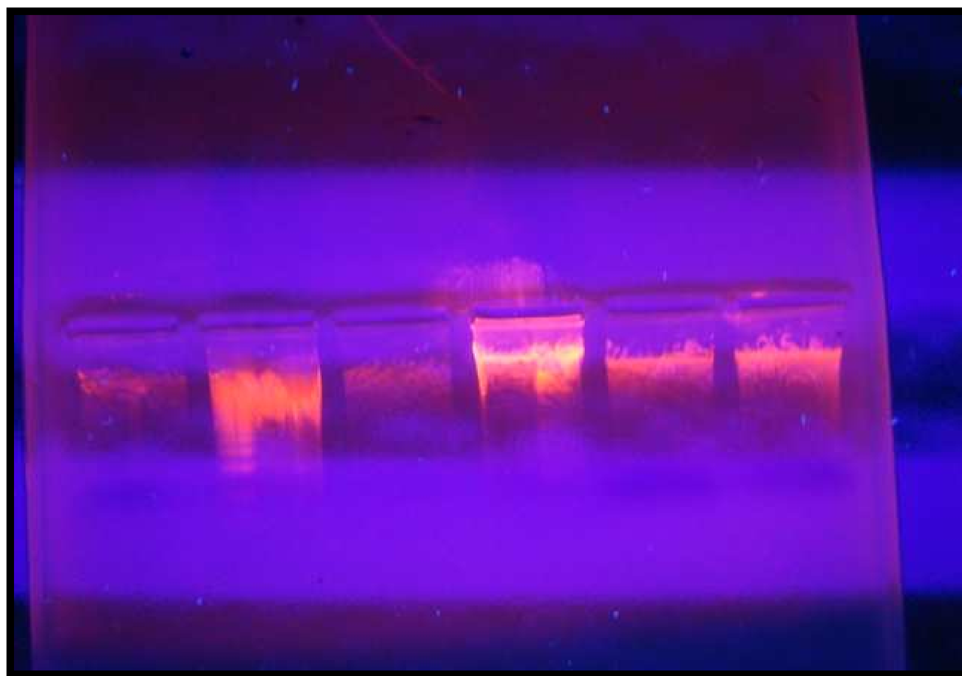
Molecular genitic study :

Polymorphism in *GSTM1* and *GSTT1* genes

The detailed analysis of polymorphisms in *GSTM1* and *GSTT1* genes is given in tables (5 and 6). among the G1,G2 and G3. the frequency of *GSTM1* was respectively 9,3,6 in G1 ,G2 and G3. In G1 one case of GSTM1 null genotype while in G2 there was 12 lack association with exposed to aramite that added with diet with OR 36,95% CI=3.92 -4.5.In G3 *GSTM1* null genotype has 13.5 fold increased risk when exposed to aramite with water . In contrast , the frequency of *GSTT1* was respectively 9,14,14 in G1 ,G2 and G3. There was one case of *GSTT1* null genotype in G1 ,G2 and G3 which appear as no significant changes when exposed to aramite with diet or water. The glutathione-S-transferases (*GSTs*) are a family of enzymes that are important in the metabolism of a wide variety of xenobiotics, including environmental carcinogens, reactive oxygen species and chemotherapeutic agents [56 and 57]. They act as phase II metabolising enzymes, catalysing reactions between glutathione and various electrophilic compounds [58]. Five classes of GST enzyme have been identified in different animal and humane. Because of their detoxification role, these enzymes and the genes encoding them may play an important role in cancer susceptibility. Although the vast majority of reactions catalyzed by the GSTs result in the detoxification products, there are a few cases in which the reaction is reversible or in which the product or a metabolite of the product is more reactive than the parent compound [58].*GSTM1* can detoxify carcinogenic polycyclic aromatic hydrocarbons in any substances that have benzene ring as center consistency such as aramite and aflatoxin, while *GSTT1* can detoxify smaller reactive hydrocarbons, such as ethylene oxide and diepoxybutane [59]). In addition, glutathione transferases may have a role in the metabolism of lipid and DNA products of oxidative stress and also in the resistance to cancer chemotherapeutic agents [60 ,61 ,62 and 63].

1 2 3 4 5 6



picture (16):photograph of agarose gel showing the high molecular weight of DNA.
Lane 1 and 2 control.
Lane 3 – 4 G2 group
Lane 5 – 6 G3 group

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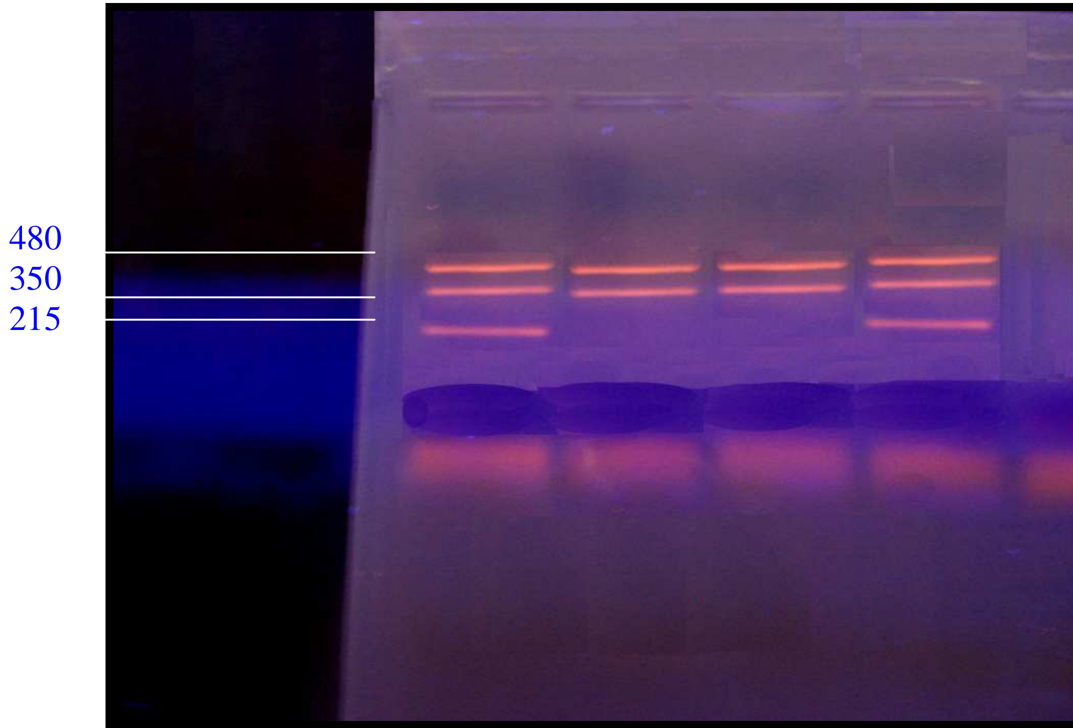

Picture (17): PCR Amplification of GSTM1 ; Albumin and *GSTT1* genes (PCR product 215bp, 350 bp and 480 bp).
Lane 1 and 4 normal .
Lane 2 – 3 null GSTM1

Table (5) distribution of polymorphism of GSTM1 gene among control and treated groups

Genotype	GSTM1(+)	GSTM1(-)	OR (95%CI)	P.value
G1	9	1	1	-
G2	3	12	36(3.92-405.915)*	0.317
G3	6	9	13.5(1.34-135.988)*	0.01

* Refer to significant differences.

Table (6) distribution of polymorphism of GSTT1 gene among control and treated groups

Genotype	GSTT1(+)	GSTT1(-)	OR (95%CI)	P. value
G1	9	1	Null	-
G2	14	1	Null	-
G3	14	1	Null	-

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التغيرات النسيجية المرضية و التعدد والوراثي الناجمة عن التعرض للاراميت في الجرذان المختبرية

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الخلاصة

مجموع 40 جرذ مختبري نوع *Rattus. norvegicus* قد قسمت إلى ثلاث مجاميع تمثلت ب G1 (10جرذان) كمجموعة سيطرة و G2 (15جرذان) عرضت للاراميت مع الغذاء لمدة 90 يوم بتركيز(5غم \1كغم عليقة) وG3 (15جرذان) عرضت للاراميت مع الماء لمدة 90 يوم بتركيز(5غم \1 لتر ماء الحنفية) .أظهرت النتائج بحصول زيادة معنوية في مستوى خمائر GPT,GOT,ACP و ALP في المجاميع المعاملة بالاراميت مقارنة مع مجموعة السيطرة .كذلك أظهرت الدراسة النسيجية حصول تغيرات نسيجية مرضية في الكبد والأمعاء وطفرات وراثية واضحة في جين *GSTM1* في المجاميع المعاملة بالاراميت مع الغذاء والماء مقارنة مع مجموعة السيطرة.

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