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Cytogenetic and biochemical studies on the effect of DDB in albino mice and their embryos.

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Abstract

Introduction: DDB (Dimethyl – 4,4/ – dimethoxy – 5,6,5/,6/ – dimethlene – dioxybi-phenyl – 2,2 – dicarboxylate) is important drug of medicine not expensive since large number of people are using it in virus B and C cases for very large periods extend to many years.

The protective of DDB on chemically induced damage was studied in primary cultures of mammals hepatocytes.

Results: This work study of cytogenetic and biochemical effect of DDB, in mice using the chromosomes of bone marrow of male and pregnant female shown some changes with liver embryos. Also germ cells of testes given non significant aberration when compared with control.

As well as some biochemical parameters in serum and tissues, shown non significant changes in nucleic acid, total protein, total cholesterol, total glucose, total triglycerides and lactate dehydrogenase (LDH). Also, enzyme analysis of liver function and kidney.

Introduction

Investigation of DDB (Dimethly dimethoxy biphenyl Dicarboxylate) is synthetic analogue of schisandrin C which is a traditional Chinese medicine since 1977 and was tried in treatment of chronic HCV in china and Egypt with encouraging results (Montasser 2000 and 2001).

DDB with the chemical structure given below has been used for the treatment of viral hepatitis and drug – induced liver injury in china for about ten years.

Liver represents the largest organ in the mammaline body. DDB had been shown to be able to protect the liver against hepatotoxins such as CCL_2, and thioacet-amide to induce liver microsomal cytoch-rome P-450 in mice and rats (Liu *et al* 1997, 1982 and Liu and Lesca 1982).

This drug was also shown to inhibit the mutagenic action of benzo pyrene (BP) and aflatoxine (AFB_1) in Ames test (Liu and Lesca 1982 & Wang 1984) and to inhibit (AFB_1) – induced hepatocarcin-ogenesis in rats (Yan *et al*, 1986).

DDB which is a synthetic analogue to schisandrin C (active ingredient in schisandra chinesis extract) showed the powerful hepatoprotective and antiviral activity (Gao *et al*, 2005). It was frequently used in Egypt in the management of chronic viral and non-viral hepatitis. It showed reduction of hepatocellular carcinoma thought the decrease of alpha-fetoprotein levels (Montaser, 1999).

Treatment options for common liver disease such as cirrhosis, faty liver chronic hepatitis. In china DDB has been tested clinically scince Liu (1979) on patients with viral hepatitis B. The results indicate that DDB markedly improve impaired liver function. Similarly Mak and Ko (1997) Suggested that DDB had hepatoprotective effect on CCL_4 – induced liver toxicity.

However Kim and Colleagues (1999) investigated the effect of DDB and observed that either single or repeated DDB pretreatment did not alter hepatotoxicity induced by CCL_4.

This work aims to study the cytogenetic and biochemical effects of DDB (Bifendate pilutes) in mice using the chromosomes of bone marrow cells, liver embryoes and germ cells.

Some biochemical parameters like Nucleic acid protein and enzymes were analyzed.

Material and Methods

Chemicals:

Definition of drug:Trade name : DDB
Generic name: Bifendate Pilules

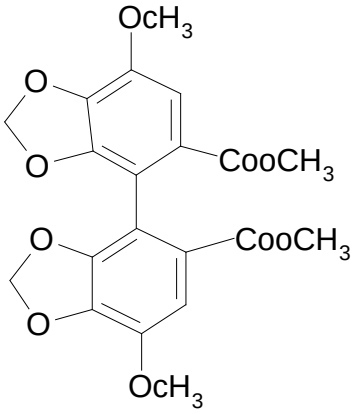
Chemical name and structural formula:

Chemical name: Dimethyl – 4,4′ – dimethoxy – 5,6,5′,6′ – dimethylenedioxy biphenyl – 2,2 dicarboxylate

Molecular formula: $C_{20}H_{18}O_{10}$

Molecular weight: 418.36

Structural formula :



Category: Antihepatitis agent

Kits: Glutamic – pyruvic transaminase GPT (ALT)

Glutamic – oxaloacetic transaminase GOT (AST)

Kit, Total protein, Cholesterol, glucose, triglycerides

Kit, Creatinina and Urea Kit (C cromastes linear chemicals S.T.)

Statistical analysis were performed using un paired t-testes (Sokall and Rohlf 1969).

Animals:

80 adult fertile male and adult virgin female Swiss albino mice 8-12 weeks old weighted between 25-30 g were used from the Department of Animal House colony of National Research Center.

All animals used in this study is divided into two main part:

First part: Cytogenetic part

Second part: Biochemical analysis

Experiment were carried out to evaluate the effect of DDB drug using different cytogenetic study and Biochemical parameters.

Animals were divided into two main equal group:

Group I : 20 animals (10 male and 10 pregnant female mice) which considered untreated mice or normal standard were gives distilled water for 30 days.

Group II: 20 animals (10 male and 10 pregnant female mice-were fed orally by DDB at 0.75 mg/kg /day for 30 days.

After the last dose animals were scarified.

A. Cytogenetic Part:

Chromosomes preparation for 40 male and pregnant female mice were caged individually and were randomly divided into two groups:

Group I : 10 male and 10 pregnant female mice served as control and were administrated with (0.25 ml) distilled water.

Group II: 10 male and 10 pregnant female mice were orally administrated with (0.75 mg/kg/ day) DDB for 30 day. (with 5 embryos for each mother).

In each mice (male and pregnant female mice) study somatic chromosomal aberration was made for bone marrow (Yosida *et al*, 1971) with liver lived embryos of mother treated DDB and control (50 embryo each group) according to (Romagnano *et al*., 1985).

In each male study germ cells (Spermatocytes) according to (Evans et al., 1964).

B. Biochemical Part:

For determined biochemical parameters for 40 male and pregnant female mice with their embryos. 40 animals were used in form of two groups as same as cytogenetic part.

The blood of mice (male and pregnant female mice) was collected and serum was separated to determine serum glucose (Trinder, 1969); Triglycerides (Fassati and Prencipe, 1982); Cholesterol (Richmond, 1973); Liver enzyme GPT (ALT) and GOT (AST) according to Reitman and Frankel (1975); Kidney enzyme Creatnine (Bartles *et al*, 1972) and Urea (Fawcett and Soctt., 1960).

Nucleic acid and total protein were determined in different tissues (Liver, Kidney, Testes and Liver embryos). DNA (Peares, 1985), RNA (Schneider 1957) and Total protein according to (Peter, 1968).

Results

I- Cytogenetic effect of DDB in mice:

1. Effect on males

The cytogenetic effect of male shown in table (1,2). The main types of structural chromosomal aberration are gaps, breaks, centromeric attenuations (C.A) and endomitosis in somatic cell of bone morrow. Table (1) showed that DDB (0.75 mg /kg / b.w) did not produce any significant change of chromosomal aberration than control in somatic cell. Table (2) shown the effect of DDB in the same male mice after 30 days in germ cells (spermatocytes) (x-y univalent, Autosmal univalent and chain). It is clear that DDB alone did not caused significant change when compared with control.

2. Effect on pregnant females:

In pregnant mice given DDB (0.75 mg/ kg/ b.w) daily for 30 days (Table 3) the result indicate non significant aberration on somatic cells (structural and numerical) when compared with untreated mice.

Table (4) shown the changes of structural chromosomal aberration in liver embryo of treated mother with DDB (0.75 mg/kg/b.w) when compared with control embryo there is non significant changes.

Mitotic index in all tables where a non significant difference appeared with treated mice (DDB) than control mice.

II- Biochemical effect of DDB in mice:

1. Changes in DNA, RNA and protein.

The results were absorved the effect of DDB on DNA, RNA and protein in different tissue of male mice (Table 5). There were some different but this diferents was non significant than control in all parameters.

As same as in pregnant female and liver embryos the effect of DDB on DNA, RNA and protein presented in table (6). The changes in all prameters gives non significant change when compared with control mother and embryo.

2. Effect of DDB in Enzymatic serum mice:

On the other hand, from male and pregnant female mice that exposure to DDB daily oral (0.75 mg/kg/d.w) for 30 days results of Enymatic serum (glucose, Triglycerides, cholesterol and LDH) (Table 7) did not give any changes than untreated mice which considered standard value.

3. Effect of DDB in liver function of mice:

In this result we studied the effect of DDB drug in tissues and serum of mice by determined the value liver enzymes GOT (AST) and GPT (ALT) in (Table 8, 9).

The result indicate there were decrease in the value of tissues (liver male, liver pregnant female an liver embryo) and serum (male and pregnant female) than control mice.

4. Effect of DDB in Kidney function of mice:

Table (10) indicate the serum of male and pregnant female mice which treated with DDB give nonsignificant data in creatinine and urea when compared with control.

Table (1): Effect of DDB on chromosomes of bone marrow (somatic cells) in male mice after 30 days)

Treatment	No of mice	No of Cells scord	Structural Aberration						Numerical aberration		Mitotic Index		
			Break	End mitosis	C.A	Gap	Total excluding gap		Hypo	Hyper	No of cells	%	Mean ± S.E.
							%	Mean ± S.E.					
Control	10	500	0.4%	0.4%	1 %	0.6 %	1.8 %	3 ± 0.866	--	--	10000	34.7 %	347 ± 15.004
DDB dray	10	500	0.4%	0.4%	1 %	0.8 %	2.2 %	3.67 ± 0.577	0.2 %	0.2%	10000	33.8 %	338 ± 18.843

Table (2): Effect of DDB on chromosomes of testes (Spermatocytes) in male mice after 30 days.

Treatment	No of examined male mice	No of cells scord	Structural Aberration			Total %	Mean ± S.E.
			X-Y univalent	Autosomal univalent	Chain		
Control	10	500	0.6%	0.8%	--	1.4%	2.33 ± 1.472
DDB dray	10	500	0.8%	0.8%	0.2%	1.8%	3 ± 1.225

Table (3): Effect of DDB on chromosomes of bone marrow in pregnant female mice after 30 days.

Treatment	No of mice	No of Cells scord	Structural Aberration						Numerical aberration		Mitotic Index		
			Break	End mitosis	C.A	Gap	Total excluding gap		Hypo	Hyper	No of cells	%	Mean ± S.E.
							%	Mean ± S.E.					
Control	10	500	0.6 %	1.2 %	1.6 %	0.6%	3.4%	6 ± 1.414	--	--	10000	27.85 %	248.5 ± 6.139
DDB dray	10	500	1%	1.4 %	1.8 %	0.8%	4.2%	7 ± 1.414	0.2 %	0.2%	10000	27.65 %	276.5 ± 5.558

Table (4): Effect of DDB on chromosomes mice liver embryo of treated mother after 30 days.

Treatment	No of mice	No of Cells scord	Structural Aberration						Numerical aberration		Mitotic Index		
			Break	End mitosis	C.A	Gap	Total excluding gap		Hypo	Hyper	No of cells	%	Mean ± S.E.
							%	Mean ± S.E.					
Control	50	2500	0.36 %	0.2%	0.64%	0.28 %	1.2 %	10 ± 3.938	--	--	50000	8.3 %	415 ± 12.247
DDB dray	50	2500	0.52 %	0.24%	0.84%	0.32 %	1.6 %	13.33 ± 5.308	0.28 %	0.32%	50000	8.16 %	408 ± 12.151

Table (5): Effect of DDB on DNA, RNA and protein in male mice after 30 days.

Treatment	Control			DDB		
	Liver	Kidney	Testes	Liver	Kidney	Testes
Total DNA mg/g	**0.418 ± 0.005**	**0.303 ± 0.064**	**0.312 ± 0.023**	**0.426 ± 0.005**	**0.309 ± 0.01**	**0. 323 ± 0.005**
Total RNA mg/g	**0.271 ± 0.033**	**0.178 ± 0.006**	**0.190 ± 0.021**	**0.276 ± 0.035**	**0.186 ± 0.021**	**0.193 ± 0.005**
Total Protein g/g	**7.041 ± 0. 161**	**4.955 ± 0.183**	**4.436 ± 0.137**	**7.126 ± 0.208**	**4.959 ± 0.118**	**4.527 ± 0.143**

Table (6): Effect of DDB on DNA, RNA and protein in pregnant female and their embryos after 30 days.

Treatment	Control			DDB		
	Liver	Kidney	Liver embryo	Liver	Kidney	Liver embryo
Total DNA mg/g	**0.369 ± 0.006**	**0.252 ± 0.009**	**0.208 ± 0.004**	**0.378 ± 0.005**	**0.282 ± 0.006**	**0. 219 ± 0.004**
Total RNA mg/g	**0.239 ± 0.012**	**0.156 ± 0.011**	**0.137 ± 0.008**	**0.245 ± 0.014**	**0.158 ± 0.008**	**0.147 ± 0.014**
Total Protein g/g	**7.027 ± 0. 188**	**4.579 ± 0.166**	**3.052 ± 0.196**	**7.111 ± 0.134**	**4.581 ± 0.161**	**3.112 ± 0.174**

Table (7): Effect of DDB on biochemical markers in male and pregnant female mice after 30 days.

Treatment	Male		Pregnant Female	
	Control	DDB	Control	DDB
Glucose mg/dl	**89.121 ± 0.586**	**89.118 ± 0. 629**	**79.83 ± 0.583**	**79.662 ± 0.587**
Triglycerides mg/dl	**66.339 ± 1.412**	**66.024 ± 1.534**	**50.8 ± 4.269**	**49.6 ± 2.782**
Cholesterol mg/dl	**193.836 ± 1.556**	**193.64 ± 1.583**	**184.328 ± 1.564**	**184.192 ± 1.639**
LDH U/L	**259.692 ± 5.004**	**258.723 ± 5.707**	**250.033 ± 5.651**	**247.095 ± 5.107**

Table (8): Effect of DDB on liver enzymes in tissues male and pregnant female with their embryos after 30 days.

Treatment	Control			DDB		
	Liver male	Liver pregnant female	Liver embryo	Liver male	Liver pregnant female	Liver embryo
GOT(AST) U/L	**52.4 ± 2.234**	**45.6 ± 1.459**	**39.5 ± 1.687**	**50.4 ± 3.159**	**43.7 ± 1.853**	**39 ± 1.956**
GPT (ALT) U/L	**58.8 ± 1.96**	**56.1 ± 2.241**	**43.8 ± 0.991**	**25.53 ± 1.251**	**52.53 ± 1.343**	**43 ± 0.861**

Table (9): Effect of DDB on liver enzymes male and pregnant female in serum after 30 days.

Treatment	Control		DDB	
	Male	Pregnant female	Male	Pregnant female
GOT(AST) U/L	**65 ± 2.222**	**63.4 ± 2.924**	**62. ± 1.757**	**61.3 ± 1.112**
GPT(ALT) U/L	**67.55 ± 1.565**	**66.2 ± 2.232**	**64.9 ± 2.616**	**63 ± 2.841**

Table (10): Effect of DDB on kidney function male and pregnant female in serum after 30 days.

Treatment	Creatinine		Urea	
	Male	Pregnant female	Male	Pregnant female
Control	**0.896 ± 0.016**	**0.788 ± 0.018**	**19.279 ± 0.378**	**16.796 ± 0.428**
DDB	**0.843 ± 0.023**	**0.733 ± 0.021**	**18.344 ± 0.38**	**15.301 ± 0.443**

Discussion

The present study showed the effect of DDB drug on mice (male, Pregnant female and their embryos). In order to investigated the role of DDB in mammals because HCV infection is wide spread problem following mainly blood trans-fusion, surgical procedures, operations and dental procedure (Donaldson *et al*, 1994).

Lenord (2005) shown that the DDB is a beneficial effect on mammal. The changes of chromosomal mice (male, Pregnant female and their embryos) non significant which mean safty and no mutagenic action was detected.

IP *et al* (2000) added that the treating mice with DDB daily oral dose did not produce any significant alteration in plasma alanine amino transferase (ALT) and sorbital dehydrogenase (SDH) activity. Also, Lui *et al* (2005) and Goa *et al* (2005) supported that the reduced elevated on ALT and AST on serum and Tissues after treated with DDB drug. Adding to Lui (1989) which said that the DDB improved the liver function in female rats as the elevated serum, GPT and GOT in liver hepatities patients have been decreased.

In carcinogen-induce DNA damage that the DDB is able to directly or indirectly protective effect (Ging and Liue, 1992) and Gao *et al* 2005). Also, Chang *et al* (2004) and Gao *et al* (2005) added that the DDB protect the inhibition of RNA which agreement with our results.

Fu and Liu (1992) reported that when normal rats were given DDB daily for 10 days, the free ribosomal protein and RNA liver increased significantly. Also, liver glycogen and blood glucose was reduced with DDB.

Mowafy (2004) investigated that the DDB when given befor meal to patients with chronic hepatitis C which is big problem in our country. The ALT and AST is lowing in serum and no effects on blood urea and serum creatinine.

The protective action of the drug mainly referred to its corrective action on protein synthesis with repair of the structure and function of damaged hepatocytes (Xa et al 1997).

This study concluded that the DDB effective observed no side effect (Salame et al 2004) which equal to our results. Also, DDB caused a significant reduction in elevated levels of all serum enzymes (ALT, AST, LDH and SDH) compared with levels of CCL_4.

This improvement of impair liver function suggests that the DDB could be used for treatment of chronic viral hepatitis B in human as it has been to reduce the main symptoms of patients and its side effect are rare and not serious (El Saway et al 2002).

In conclusion, the present data indicate that oral administration of DDB, have a beneficial effects on damaged liver cells to prevent lipid peroxidation and improve antioxidant enzyme activiles.

The data obtained from study revealed that DDB commediate its biochemical effects to protect action against liver.

The toxicity of DDB is very rare No teratogenic or mutagenic action was detected No untoward effects of DDB have been observed. DDB is not expensive with no side effects.

References

1. **Bartles H, Bohmer M and Herirli C (1972):** Creatinine coloimetric kinetic Method Clin – Chem. Acta, 37, 193 – 195.
2. **Chang SM, Kuhn J, Wen P, Greenberg H, Schiff D, Conrad C, Fink K, Robins HI, Cloulghesy T, De Angelis L, Rozier J, Hess K, Dancey J and Prados MD**

(2004): Phase 1 / Pharmacokienetic Study of CCL-779 in Patients with recurrent malignant glioma on enzyme – inducing antiepileptic durgs 1-Investigational New drug, 22 (4):427–432.

3. **Donaldson P, Doherty D and Llnder hill J (1994):** The molecular genetic of autoimmune liver disease. Hepatology, 20:225 – 230.
4. **El- Beshbishy HA (2005):** The effect of Dimethyl Dimethoxy Biphenyl Dicarobxylate (DDB) against Tamoxifen – induced liver injury in Rats: DDB use Is curative or protective. J. of Biochemistry and Molecular Biology, 38 (3): 300 – 306.
5. **El-Saway SA, El-Shafey AM and El-Bahrawy HA (2002):** Effect of dimethly diphenyl bicarboxylate on normal and chemically injured liver. Estern Mediterranean health Journal, 8 (1).
6. **Evans E P, Breckmon G and Ford CF (1964):** An-air drying method for meiotic preparation from mammalian tests. Cytogentics, 3: 289 – 291.
7. **Fassati P and Prencipe L. (1982):** Trigly cerides Enzymetic colorimetric method. Clin. Chem., 28: 2077-2081.
8. **Fawcette JK and Soctt JT (1966):** Urease – Berthelot Method J. clin path, 13: 156 – 159.
9. **Fu T and Liu G (1994)** : Protective effects of dimethy L – 4.4$^{/}$ – dimethoxy – 5,6,5$^{/}$,6$^{/}$ – dimethylene dioxybiphenyl – 2, 2$^{/}$ dicarloxylene on damages of isolated rat hepatocyte induced by carbon tetrachloride and D- galactosamine. Biomedical and environmental Science, 5 (3) : 185 – 194.
10. **Gao M Zhang J and liu G (2005)** : Effect of dipheuyl dimethyl bicarloxylate on cancanavalin A- induced liver injury in mice. Lin – Int , 25 (4) : 904 – 912.
11. **IP SP, yiu H Y and KO KH (2000):** Differential effect of schisandrin B and dimethyl diphenyl bicarloxylate (DDB) on hepatic mitochondrial glutathione redo status in carbon tetrachloride intoxicated mice. Mol cell Biochem 205 (1-2): 111-114
12. **Kim S N, Kim sy, yim HK, lee w y Han K-S ,Kim SK, yoon N y and Kim y c (1999):** Effect of dimethyl – 4,4$^{/}$ – dimethoxy - 5,6,5$^{/}$,6$^{/}$ dimethylene dioxybiphenyl – 2,2$^{/}$ dicarboxylare (DDB) on chemical – induced liver injry. Biol pharm Bul I , 22 (1) : 93 – 95.
13. **Leonard A (2002):** Hertable chromosome aberrations in mammals after exposure to chemicals. J. Radiation and Environmental Biophyscis, 13 (1) : 1 – 8.
14. **Liu G T, wamg GF, wei H L, Bao TT and song ZY (1979):** Acomporison of the protective actions of Biphenyl Dime thyl Dicarloxylate , Trans – stillene, Alcoholic extracts of Fructus schizandra and ganoderma against experimental liver injury in mice. Acta pharm . sin, 14: 598 – 604.
15. **Liu K T and Lesca P (1982):** Pharmacological properties of dibenzo (a) cyclooctine derivatives isolated from Fructus schizandra chinesis III. Inhibitory effects on carbon tetrachloride – induced lipid peroxidation metabolism and covalent binding of carbon tetrachloride to lipid. Chem. . Biol . Interact, 41: 39 – 47.
16. **Liu KT, Cresteil T, columelli S and Lesca P (1982):** Pharmacological properties of dibenzo (a.c) cyclooctenc derivatives isolated from fructus schizandra chinesis II. Inductoon of phenobarbital. Like hepatic mono oxygenase Chem. Biol. Interact, 39: 312 – 330.
17. **Liu GT, Li y wei H L, Zhang H, Xu J y and yu LH (2005):** Mechanism of protective action of bicyclol against CCL induced liver injury in mice. Liver internationall, 25, (4) : 872 – 879.
18. **Mak DH and Ko KM (1997).** Alteration in susceptibility to carbon tetrachloride and hepatic antioxidant detoxification system in streptozotocin – induced short – term diabetic rats : Effect of insulin and schisandrin B treatment – Moleeular and cellular biochemistry, 17 : 20 (1-2) 225 – 232.
19. **Mawafy T (2004).** Clinical evaluation of efficacy of DDB on patients with chronic hepatitis C Al Ahrame Company for drugs. Mol Cell Biochem 205 (4-2): 111-114.
20. **Montaser M F (2000):** Aclinical and Laboratory study of DDB in treatment of chronic hepatitis C : 2 comparative studies. Ain shams Medical, J, 51 (1,2&3) : 209 – 223.
21. **Montaser M F (1999):** Aclinical and labortory role of DDB in treatment of chronic hepatitis C, a preliminary report in Egypt. Ain shams Med. J, 50 (12 - 12) : 1015 – 1023.
22. **Montasser m M F (2001):** Clinical and laloratary studies of DDB in treatment of chronic Hepatitis Apilot studyin Egypt. Combination therapy with Amantadine Hydrochloride, Ain shams medical J. 52 (1,2&3) : 125 – 142.
23. **Peares AGF (1985):** Histochemistry theoretical and Applied, – volume two : Analytical technology , churchil livingston 4th ed. Edinburgy London, Melbourne and New York.
24. **Peter T (1968):** proposals for standardization of total protein colorimetric

method assays. Clin. Chem., 14 (12) : 1149 – 1159.

25. **Qing w and Liu G (1992):** Protective effect of dimethyl – 4,4′ – dimethoxy - 5,6,5′,6′ – protective effect of dimethyl – 2,3′ – dicarboxylate (DDB) against carcinogen induced ratinuclear DNA damage. Biomed Environ Sci, 5 (3): 201 – 207.
26. **Reitman A and Frankel S (1957):** Glutamic – pyruvic trans aminase (GPT) and Glutamic oxaloacetic transaminase (GOT). Am . J Clin-Path 28 : 56 – 63.
27. **Richmond W (1973):** Cholesterol enzymatic colorimetric method. Clin . Chem . 19 : 1350 – 1355.
28. **Roeschlau P, Bernt E and Gruber w (1974):** Enzymatic Determination of total cholesterol in serum: Z klin chem. Klin Biochem 12 (5) : 226 – 231 .
29. **Romagnano A, King A w, Richer CL and Perrone M A (1985):** Adirect technique for the preparation of chromosomes for early enquine embryos. Can, J. genet. Cytol 27 : 365 – 369.
30. **Salama HM, Amer AR, Hammed OM, and El-Sayed WF (2004):** Effect of DDB Monotherapy and in Combination with amantadine Hydrochloride and Ribavirin in patients with chronic Hepatitis C virus infection. Sci. Med. J. escme 16, 1:9 -16.
31. **Schneider WC (1957):** "Determination of nucleic acids in tissues by pentose analysis : In "Method enzymology" (Edited by colowick S.P. and Kaplan. N.O.) Academic Press. New York, 680-684 .
32. **Sokall RR and Rohlf F J (1969):** Biometry by W.H. ferman and Company Chapter, 9: 204-252.
33. **Trinder P (1969):** Glucose Enzymatic colorimetric method. Ann. Clin. Biochem, 6, 24-28.
34. **VanuKumar MR, and Lathal MS (2002):** Hepatoprotective effect of the methanolic extract of Curculigo orchioides in CCL_4 treated male rats. Int. J. Pharmacol, 34: 269 – 275.
35. **Wang CF (1984):** Mutagenetic and anti-mutagenetic effect of DDB Report on National Meeting for pharmacological society 1984.
36. **Yan RQ, Chen ZY and Gin GZ (1986):** Effect of Bifendati and three Chinese traditional medicinal herbs on the AFB_1-induced hepatocarcinogenesis in rats. J. Oncol, 5: 141-144.
37. **Yosida TH, Truchiya K and Mariwaki K (1971):** Frequency of chromosome polymorphism of Roltus Rattus collected in Japan. Chromosoma, 33: 30 - 40.
38. **Zhanq BH, Gonq DZ and Mei MH (1999):** Protection of regenerating liver after partial hepatectomy from carbon tetra-chloride hepatotoxicity in rats: role of hepatic simulator substance. J. Gastroc-uteral Hepatol, 14 (10): 1010 – 1017.

دراسة التأثير الوراثى الخلوى و الكيمياء الحيوى لعقار ال د د بى (DDB) على الجرزان البيضاء الصغيرة و أجنتها

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نظرا لانتشار فيروس سى و بى بالكبد و لقد انتشرت أدوية كثيرة لعلاجه و لأنها غالية الثمن و لها تأثير فلقد قمنا بدراسة عقار ال د د بى (DDB) وتاثيره على الثدييات لانه غير مكلف ويستخدم لفترة طويلة . ولقد قمنا بالدراسة على جزين جزء وراثة خلوية وجزء كيمياء حيوية.

الجزء الأول الدراسة الخلوية قمنا بدراسة كرموسومات الفئران البيضاء الصغيرة لكل من الذكور والإناث الحوامل فى نخاع العظم ووجد انه لا يوجد تأثير بالمقارنة للمجموعة الضابطة الغير معاملة وايضا دراسة كرموسومات الكبد بالنسبة لاجنة الإناث الحوامل المعاملة بال (DDB) وجدت انها لم تتأثر تأثير معنوى . وبالنسبة للذكور قمنا بدراسة كرموسومات الخصية ووجدت أيضا أنها لم تتأثر بالمقارنة بالمجموعة الغير معاملة .

الجزء الثاني قمنا بدراسة التأثير الكيميائي الحيوي للعقار (DDB) على خلايا بعض الأعضاء (الكبد والكلى والخصيتين وكبد الاجنه) والدم ووجد انه لا يوجد تغير فى الحامض النووى (د ن ا ، ر ن ا) والبروتين والكلوستيرول والجلوكوز و الترى جلسرين والكتات دهيدروجينز ولافى أنزيمات الكبد ولا الكلى من هنا وجد ان عقار (DDB) ليس له تأثير ضار ورخيص الثمن وممكن استعماله بأمان .