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The effect of Nigella sativa oils on hyper lipidemia in the human.

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Introduction:-

One of the most important cause of death , all over , the world is ischemic heart diseases & C.V.A.. The major factor in the pathology of these two diseases is atherosclerosis, in which , diabetes , hypertension & hyper lipidemia play an evident roles in its causes[(1)(2)] .

For these very important reasons, scientists try their best to dissolve this problem ; once they try to reduce hyper lipidemia (all types of lipid) through regulation of diet , others try to use medications with or without diet regulation [(3)]. However, medications used (for example statins ,nicotinic acid , lopid , tricor etc ……)have limited effects in reducing lipid level ,since it needs long time , can not be used in all conditions, besides, they are not free of risks as a side effects .

Therefore , in the last decades , scientists turned their attention toward using harmless herbs since, these herbs posses pharmacological principles. Besides , traditionally these herbs are widely utilized to improve human health through curing numerous diseases. Example for these herbs are fenugreek & nigella sativa[(4)(5)(6)] .

According to the world Healt Organization (WHO) reports, 70-80%, of the people over the world , have a great confidence in traditional medical herb for primary health cure. For these reasons , 30% of all modern drugs are derived from plants[(7)] .

One of these important plants that play a big role as medication is Nigella sativa mainly its dried seeds[(8)].

Nigella sativa is an annual herbaceous plant from Ranunculaceae family producing small black seeds, which have characteristic aromatic odor & taste[(9)].

Besides, its uses as a spices & condiment , it is one of important plants seeds that was used as a traditional medicine as a galactagogue , carminative , laxative besides their anti – parasitic properties[(10)] . Recently , animal studies have shown that extract of N.sativa have many therapeutic effects such as gastrotection, anti malignant effect[(11)] , & anti oxidant[(12)].

The black seeds have different constituents such mucilage , crude fiber , alkaloid , sugar resins , saponins & proteins[(8)]. Besides , they have high content of unsaturated fatty acids[(13)].

One of these medical uses of N.sativa seeds is treatment of hyper lipidemia[(4)].

Many scientist used the crude crushed N.Sativa seeds, orally , in the treatment of the hyper lipidemia . This treatment had been used in experimental animals[(14)] & in human being[(15)].

However the active ingredient , in N. Sativa seeds , is still obscure , besides , the mode of action is unknown.

Aim of study :-

1- Detection of active ingredient of the N.Sativa constituents that considers the important factor in lowering lipid level in the body of the human being .

2-A trial to know the mode of action (mechanism of action) of these seeds by using histochemical methods ,for detection of activity of lipo – protein lipase in the liver of the rat.

- ***material & method :-**

1-chemical analysis of N.sativa seeds:

N. sativa seeds had been purchased from local market in Baghdad. The seeds had been authenticated as N.sativa seeds, of family of ranueulaceae ,by specialist potaniest, then they had been cleaned .

The instrument used for extraction of seeds is soxhelt apparatus.Here Ramadhan et al[(16)] had been followed,

used 95% hexane for extraction

After extraction procedure had been finished &isolation of N.sativa oil had been obtained , it was characterized by infra- red spectroscopic technique (Tensor 27 – PRUKER). The remaining material of the N.sativa (after oil extraction) had been collected &dried.

This procedure had been done in the research laboratory of ministry of science & technology in Iraq.

2-Experimental study (animals & methods):-

Swiss albino rat, had been used in this study .The no. of rats used in the study was fifty (50) male rat. The average weight of the rat is 250 gm.

These animals had been divided 5 groups, 10 rats for each & as follow in table no.1:-

Table (1)

1st group	2nd group	3rd group	4th group	5th group
Received 3cc of Distelled Water for 1 month	Received 18 Crushed Crude N.stiva seed (300mg/Kg. body weight[5]) for 1 month	Received0.4ml of N.sative oil orally/day[17] for one month	Received Atrovastin tab (1tab 20mg/tab) daily for one month	Received remanant material of extraction in adose of 300 mg/1kg.body weight for 1month.

Groups of experimental animals (rat).

All experimental rats in all 5 sub groups had been exposed for histochemical detection of the activity of lipoprotein lipase enzyme in the liver of the rats using tween method as prescribed by Gomori 1952[18][19]. Here tween substrate (tween 80)[20] had been used .

2-**Patient and method:-**

This study was done in the period between September 2013 -February 2014 . It included 45 patients , aging 40-50. Thirty-six patient, out of the whole experimental patients , were hyperlipidemic with same complication of hyperlipidemia (Hypertention , ischemic heart disease , transient ischemic attack . etc …).the others 9 .Persons are normal (had normal lipid profile).

These patient had been divided into 4 groups , as summarized in table (2) :-

Table (2)
Groups of patients

Group	control	1st groub	2nd group	3rd group	4th group
No. of patients	Patient (9 in no.)	Patient (9 in no.)	Patient (9 in no.)	Patient (9 in no.)	Patient (9 in no.)
	Received capsule filled with o.5 gm sugar(placeb) t.d.s for 4 months	Received crushed crud N.sativa seed (encapsulated) in a dose of 1cap. 0.5 gm t.d.s for 4month	Received N.sativa oil inform of drops in dose of 3 macro drops t.d.s orally for 4 month	Received remnant of extraction of oil from N.sativa seed encapsulated in a dose of 0.5 gm t.d.s. for 4 months	Received atrovastin tablets in a dose of tablets dialy (40mg/tab) (TAD pharma GmbH heinz-lohmann-S tra Be 5 27422 cux haven Germany) for 4 months.

Each Patient in this experiment exposed monthly for blood examination for lipid Profile (including cholestrol , triglyceride ,HDL , LDL, & VLDL)monthly. These examination had been done in the teaching lab of medical city – Baghdad.

Note:- the average of lipid profile in the 4 hyperlipidemic sub groups was aS follows:

- Cholesterol : 406+15 mg/dl
- Triglycoride : 340 ∓ 20 mg/dl
- HDL 45∓ 4mg/dl
- LDL 65 ∓ 5 mg/dl.
- VLDL :62 ± 3mg/dl
  - Estimation of Results obtained :
  - Statistical analysis :-
- Student T- test was applied to estimate the significane of changes that had been obtained in patients , by comparing the mean & standard deviation of each subgroup

This analysis had been detected the significance of the results obtained among patients involved in the experiment.

Note: - * 0.05 significant .

** 0.01 highly significant.

*** 0.001 very highly significant.

Regarding the results obtained from experimental animal; mainly the intensity of reaction of lipo – protein lipase which had been appeared as discolouration at the site of the enzyme , was subjectively assessed by double blind assessment . The activity of this enzyme had been measured using the method of (+) as appeared in table (3):-

Table (3)

Intensity of activity of lipoprotein lipase enzyme.

Activity of lipase enzyme i. e intensity of reaction	Presentation as +
No enzyme activity	-
Normal enzyme activity	+
Moderate enzyme activity	+ +
Strong enzyme activity	+ + +

Note:- normal enzyme activity indicates lipase enzyme activity in normal subject .

Results:

The results obtained from this study was arranged in a sequence as that in the material & methods &as follows.

- Results of chemical analysis of N.sativa seeds :-
- The extraction of N. Sativa oil (which had faint green – yellowish color) revealed the following constituents as shown in table (4) :-

Table (4)

Constituents of N.sativa oil & their percentage.

Constituent	% Range w/w
Linoleic acid	44.7 – 56
Oleic acid	20.7 – 24.6
Linolenic acid	0.6 – 1.8
Arachidic acid	2 – 3
Palmitolic acid	3
Eicosadieneic acid	2 – 2.5
Palmitic acid	12 – 14.3
Stearic acid	2.7 – 3
Myristic acid	0.16
Sterols	0.5

Each 1 kgm of dried N.sativa seeds gives 200 mls of fixed oil while the remnant dried part weights about

620 gm.

Results of lipo – protein lipase activities in the liver of the experimental rats:-

The intensity of reaction of lipase enzymes (which appeared as brown –black color precipitate) in different experimental group could be shown in table (5) & in fig A&B&C:-

Table (5)

Intensity of reaction of lipoprotein lipase enzyme in the different group of experimental animals.

Experimental group	Degree of intensity of reaction	Figure
1st group	+	Fig.A
2nd group	+ + + * * *	Fig.B
3rd group	+ + + * * *	Same as Fig.B
4th group	+ + * *	Fig.C
5th group	+	Same as Fig.A

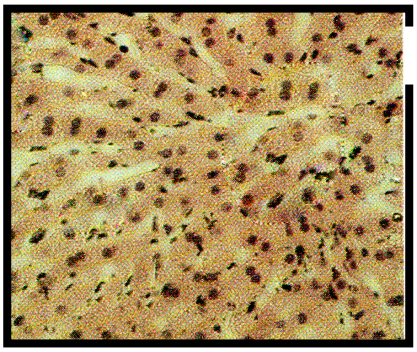

Fig. A

Lipoprotein lipase enzyme, activity in 1st & 5th groups of experimental animal.

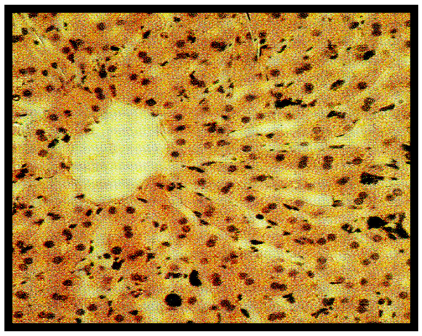

Fig. B

Lipoprotein lipase enzyme activity in 2nd & 3rd groups of experimental animal.

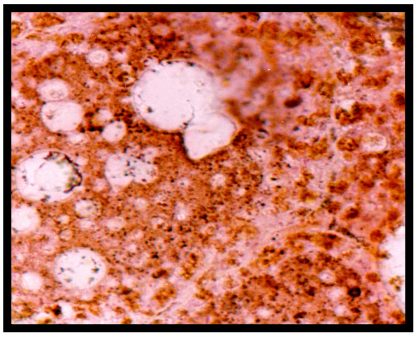

Fig. C

Lipoprotein lipase enzyme activity in 4th groups of experimental.

Lipoprotein lipase revealed strong activities in the 2nd & 3rd group while 4th group showed moderate intensity of enzyme reaction. However 5th group of animal elicited the same enzymatic activity as control one (1st group), which is the normal lipo-protein lipase activity .

Table (6)
Duration of experiment value of deferent types of lipid profile & the significance of results obtained in different groups of experimental human being.

Group of patients	duration	Lipid profile					Significancey
		cholesterol	Triglyceride	HDL	LDL	VLDL	
Control group	1ST month	180 20mg/dl	135 11	50 2	38 1	34 3	Not significant
	2nd month	190 18mg/dl	132 7	52 3	36 2	36 3	
	3rd month	195 25mg/dl	136 8	51 5	37 6	34 5	
	4th month	198 18mg/dl	130 5	54 3	35 3	37 1	
1st Experimental group	1ST month	360 20mg/dl	280 15	52 1	59 1	58 3	Very highly significant ***
	2nd month	300 15mg/dl	230 13	60 5	50 4	50 3	
	3rd month	257 25mg/dl	202 10	65 3	42 1	44 5	
	4th month	200 18mg/dl	159 5	75 2	35 2	38 1	
2nd Experimental group	1ST month	350 39mg/dl	278 18	55 2	58 4	59 3	Very highly significant ***
	2nd month	290 20mg/dl	237 13	61 2	51 2	51 2	
	3rd month	220 25mg/dl	205 18	66 4	42 2	43 3	
	4th month	195 10mg/dl	165 7	72 5	34 3	39 4	
3rd Experimental group	1ST month	390 17mg/dl	310 11	45 4	65 4	62 3	Not significant
	2nd month	385 15mg/dl	310 16	45 7	64 5	63 1	
	3rd month	382 25mg/dl	315 12	43 3	62 5	60 4	
	4th month	380 11mg/dl	301 20	46 1	66 7	59 2	
4th Experimental group	1ST month	360 35mg/dl	285 3	47 2	62 1	60 4	Highly significant **
	2nd month	339 29mg/dl	260 8	50 1	3 57	57 5	
	3rd month	312 20mg/dl	251 16	54 1	54 1	55 2	
	4th month	290 18mg/dl	228 11	60 3	46 4	50 5	

-Results of patients & methods:-
The effects obtained from treatment of the four experimental human groups by N.sativa oil , on the five subgroups of lipid profile, could be summarized in table (5):-
Note : the normal value of – cholesterol 150 – 250 mg/dl =3.9-6.5mmol/L
-Triglycerides 65-180 mg/dl =0.9-2.4mmol/L
-HDL 35-70 mg/dl =0.9-4.4mmol/L
-LDL < 40 =1.8-4.3mmol/L
-VLDL < 40 =< 0.53mmol/Lion
From this table , it was so obvious that N.sativa crude seeds & N.sativa
Oil revealed very highly significant reduction in the level of all subgroups of lipid profile till normal within 4 months of treatment , excent HDL was revealed highly significant increment . (i.e these results obtained in the patients of 1st & 2nd experimental groups).
Patients of the 3rd group showed no changes in the level of all subgroups of lipid profile (similar to the results of the control group)
4th group experimental patient detected highly significant decrement in lipid profile within the duration of treatment .

Discussion & Conclusion:-
Since atherosclerosis is the main cause of major pathology that lead to death , & hyperlipidemia is one of the major factor in pathogenesis of atherosclerosis[(1)(2)] , treatment of hyperlipidemia attracts the attention of many scientist to solve this problem.
Although , there are many antihyperlipidemic medication the scientists try to find their goal in medical

plants. One of the important one is N.sativa seeds .The important active ingredient factor of N.sativa seeds is the oil of the seeds .

However , the mode of antihyperlipidemic action of this herbs seeds is still obscure .

Cholesterol is transported from intestine to the liver[22]. ultimately, cholesterol is excreted in the bile as free cholesterol or as bile salts . Besides, cholesterol could be converted into LDL & VLDL, within the liver[23] . For this reason hepatic cells enzymatic activities play an important role in controlling the level of lipids in the body .in this study , the lipoprotein lipase enzyme revealed very highly significant increase in activity when N.sativa seeds oil or crude crushed seed had been given to the experimental animal (Fig B & C).

Besides N. sativa seeds oil revealed superior action as an antihyperlipidemic treatment than chemical drugs used for this purpose (table 5).

Also N.sativa seeds oil has many beneficial effects other than lowering the lipids in hyper lipididemic patient like availability, cheapnest safety & with no or very little side effect while anti – hyperlipidemic drugs have so many side effects when used .

Recently, marvollous benefit of usage N.Sativa oil as an anti hyper lipidemic medication superior to the statin drugs , that statin group of drugs is contra indicated in pregnancy & lactation[24] , while N.Sativa is very safe ,besides , its usage as a galactagoge to newly delivered women[10].

From this study,it is advisable to use herbal medication(i.e. N.sativa seeds oil)in the treatment of hyperlipidemia as a first choice other than antihyperlipidemic drug, since its effect is superior to the other, besides it is cheap, available ,& approximately free of side effect.

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