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EVASION OF HEPATIC TISSUE DAMAGE THROUGH AMELIORATIVE EFFECT OF FLAXSEED OIL: AN EXPERIMENTAL RESEARCH ON ALBINO RATS (MALE)

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Abstract:

Objective: *Hepatic damage is created by Lipofundin which is used in parenteral therapies and is a soya-bean based lipid emulsion. This research was performed to know preventive effect of flaxseed oil on the hepatic damage.*

Material and Methods: *Our research was of experimental nature conducted at Allied Hospital, Faisalabad (February, 16 to January, 17). This research is done to determine effect of the flaxseed oil on lipofundin induced (hepatotoxicity). From animal house, 32 male adult-albino rats were taken & classified in 4 equal groups. First group was control group & given (flaxseed oil) three ml per kg intraperitoneal on daily basis for ten days & only sacrificed on the 11th day. Second group B, Lipofundin three ml per kg intravenously on daily basis for ten days & only sacrificed on 11th day. Third group C, Lipofundin two ml per kg intravenously on daily basis for ten days & only sacrificed on 21st day. Fourth group D, Lipofundin two ml per kg intravenously for a period of ten days and also followed by (Flaxseed oil) three ml per kg intraperitoneal for a period ten days & only sacrificed on 21st day.*

Results: *Hepatic tissue damage was found to be restored by flaxseed oil. This damage was caused by (Lipofundin administration).*

Conclusion: *Hepatic tissue damage is caused by (Lipofundin Flaxseed oil) & Lipofundin. The flaxseed oil has an ameliorative effect on it. So by using it, we may avoid hepatic tissue damage which is caused by (Lipofundin) and is used for (parenteral therapies).*

Keywords: *Lipofundin, Hepatotoxicity, Flaxseed oil.*

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INTRODUCTION:

Those patients who are suffering from poor nutrition & who are not able to take orally, (parenteral nutrition) is given to them. Because improper taking of nutrients may cause vulnerability in many nutritional-related diseases & enhanced mortality rate. Inadequate nutrients include both macronutrients & micronutrients [1]. The (parenteral nutrition) should have proteins, carbohydrates, fats, vitamins, electrolytes & fluid with suitable number of trace elements having capability of fulfilling daily needs of body with respect to weight & height of patient [2].

Sources of energy are fats & lipids in therapies which are given parentally so doing a task in avoiding energy shortages [3]. Lipids may be given in largely spreading infections, severe burns & wounds linked with multiple trauma [4]. The fats are available in emulsions that are made-up of long and medium chain triglycerides respectively LCT & MCT in which necessary fatty acids are included.

Lipofundin is one of such emulsion out of twenty percent used mostly in the world and is soya bean-based (fat emulsion) containing both (LCT) & (MCT) [5]. For oxidative stress, (Lipofundin 20 percent) was observed responsible also including the (hyperlipidaemias) & (atherosclerotic lesions). It was shown in the experiments conducted on rabbits [6]. The (hyperlipidaemia) causing by (Lipofundin 20 percent) might be because of large level of (triglycerides) in emulsions based on soya bean [7]. Including Lipofundin, the total (parenteral nutrition) was observed causing (hepatic steatosis) [8]. For its seeds, (flax plant) which is lignum ustitissimum is normally cultivated in the whole world [9].

Flaxseeds are used to get (flaxseed oil) and is used as a (nutritional supplement) in the whole world. If we take it in routine diet, it is popular for its (cardio protective properties) [10] and (hypocholesterolaemia) effects of this oil are very popular [11]. Taking this oil enhances (high density lipoproteins) and it also minimizes (low density lipoproteins) which plays a role in avoiding (cardiovascular diseases) provided we add it in daily food [12].

The supplementation of (flaxseed oil) showed enhanced (anti-oxidant status) of the liver in all obese rats which is protective task completed by flaxseed. It is working against (oxidative stress) which is due to fat rich diet [13]. The flax plant is cultivated normally in western Canada having flowers of blue colour [14]. This plant has seeds of dark brown colour & their shape is oval [15].

The flaxseeds are from harvest and are full of (fatty acids) omega-3 & 6 with phytoesterogenic-lignans with inclusion of secoisolariciresinol-diglucoside [16]. The oil is extracted from seeds with the help of a (cold pressure procedure) [14].

MATERIAL AND METHODS:

Our research was of experimental nature conducted at Allied Hospital, Faisalabad (February, 16 to January, 17). For this study, 32 (male albino rats) from animal house were taken randomly for experiment & divided in 4 equal groups having 8 animals in each in which inclusion criteria was healthy rats. The diseased rats were not included.

First group was control group & given (flaxseed oil) three ml per kg intraperitoneal on daily basis for ten days & only sacrificed on the 11th day. Second group B, Lipofundin three ml per kg intravenously on daily basis for ten days & only sacrificed on 11th day. Third group C, Lipofundin two ml per kg intravenously on daily basis for ten days & only sacrificed on 21st day. Fourth group D, Lipofundin two ml per kg intravenously for a period of ten days and also followed by (Flaxseed oil) three ml per kg intraperitoneal for a period ten days & only sacrificed on 21st day.
The macerated, fresh dried flaxseeds were taken for extracting the oil & seeds were also soaked in the (petroleum ether) for 7 days. After it, seeds were filtrated & then collection of (flaxseed oil) by the air drying filtrate [17].

The (Lipofundin 20 percent emulsion) that is provided commercially was used as Germany, Melsungen, Braun, Melsungen AG [5].

The under-study 32 (albino rats) were divided in 4 as A to D. The rats marked & kept in 4 cages having label of title of group with the researcher name. The weight was noted on first & last day. Anaesthetization of the rats was carried out. In supine position, we kept anaesthetized rats on dissection slab.

The liver was identified by opening abdomen, liver was exposed & removed by detaching from (diaphragm). It was washed to remove blood & weighed with digital balance (Sartorius of model no T E-214-S). It was kept in ten percent formalin solution in (labelled containers) for a period of 24 hours. The pieces of tissue (3 to 5 mm) were cut from (median lobe) of liver & kept in ten percent (formalin solution) for a period of two days for the sake of fixation. For processing, liver tissue was trimmed for

affixation and size. Five micrometre thick dry slices were obtained. Dryness was maintained at room temperature.

The slides were stained, hydrated through (haematoxylin) & for light microscopy eosin. For regular vaculation and arrangement; hepatocytes were checked. Congestion was observed through central vein. Moreover, (periportal polymorph nuclear infiltration) was looked for the grading of (periportal inflammation) as moderate, mild, severe and absent. Under (light microscope) with PAS stain, (basement membrane continuity) was looked in basement membrane around which there is central vein.

The obtained data was analysed by (SPSS). The mean as ± SD was measured for all (quantitative parameter) in a tabularized shape & parameters among groups were compared by applying (one-way ANOVA). For multiple comparison among groups, (post hoc Tukey test) was applied and (light microscopic) examination was performed.

At (X400 magnification) 2 slides from every animal were studied. Percentages of data were measured for (qualitative histological variables) like (basement membrane continuity), vacuolation, periportal inflammation, (hepatic lobular pattern) & (central vein congestion). For statistical significance in groups, Chi-square test was utilised ($P < 0.05$).

RESULTS:

The range of initial weight of all 32 animals was (175 - 225 grams). At the end of experiment, final weight was noted & found the mean ± SD of weight of all groups i.e. from A to D was found as (226.12 ± 10.83, 178.75 ± 16.52, 187.37 ± 5.64 & 207.87 ± 10.39 grams) respectively at time of sacrifice. A clear statistical variation was shown by (one-way ANOVA) in mean of last weight of animals. Hepatic tissue damage was found to be restored by flaxseed oil. This damage was caused by (Lipofundin administration). Detailed outcomes have been shown in tabular and pictorial form below:

Table – I: Comparison of mean weight of animal among different groups

Parameter	Group "A"		Group "B"		Group "C"		Group "D"		*p*-value
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	
Initial Weight of Animals (gms)	185.3	11.4	186	13	179	4.79	186.9	12.7	0.472
Final Weight of Animal (gms)	226.1	10.8	178.8	16.5	187.4	5.64	207.9	10.4	<0.001

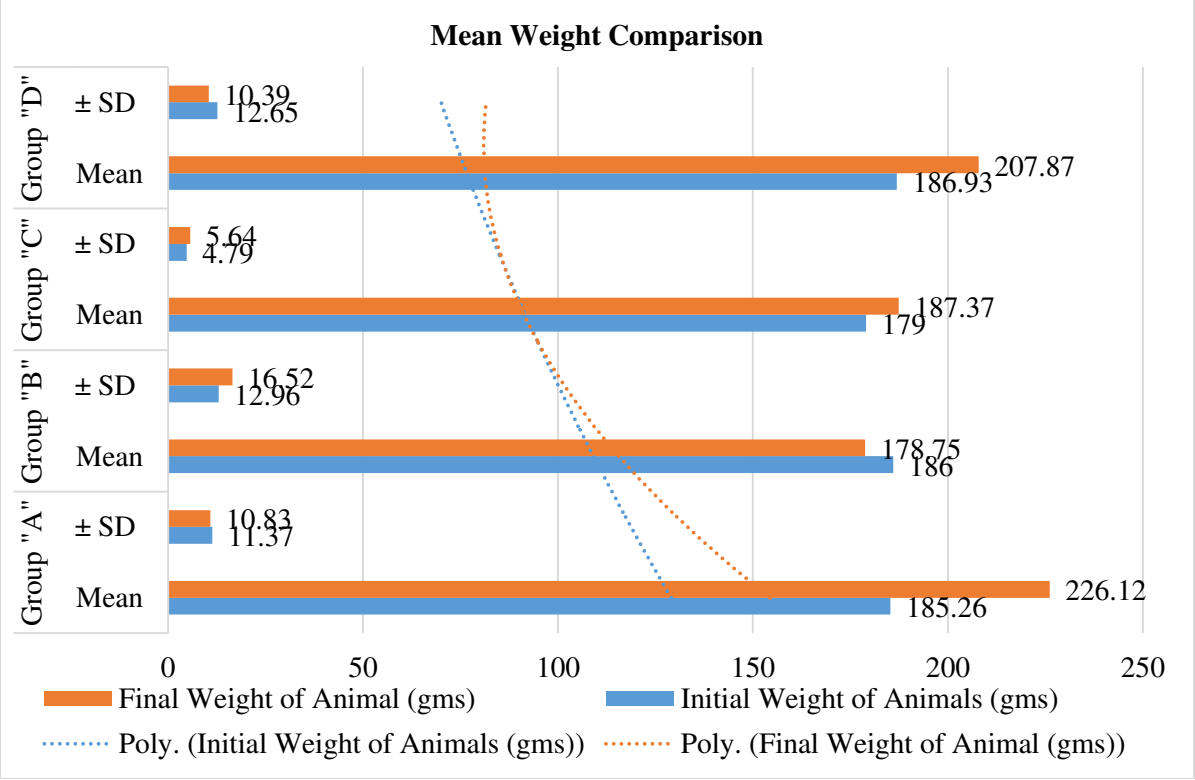
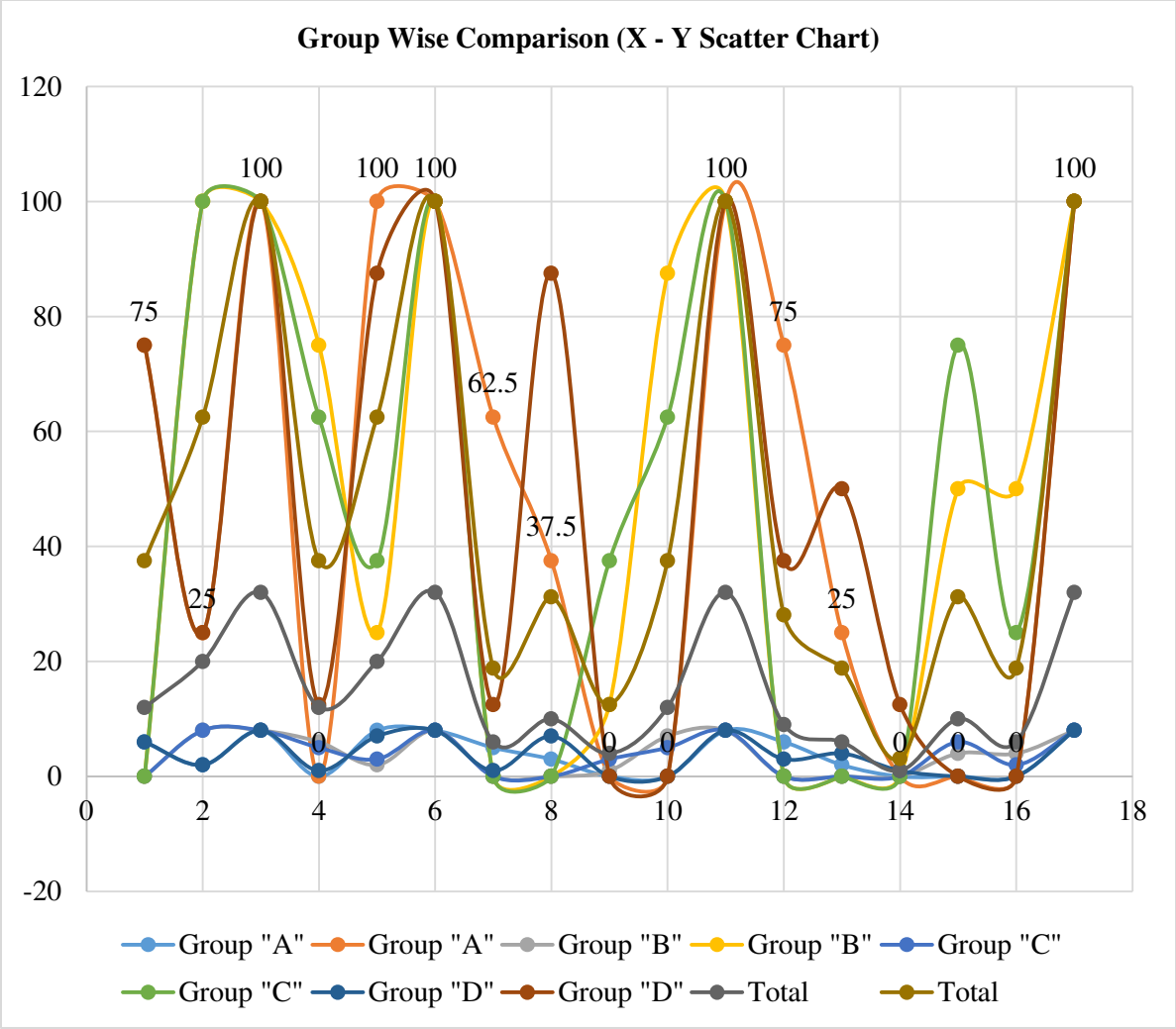


Table – II: Tukey HSD test showing multiple comparisons of final weight of animals among groups A, B, C and D

(I) Groups	(J) Groups	Mean Difference (I-J)	Std. Error	*p*-value
A	B	47.375	5.75786	<0.001
	C	38.75	5.75786	< 0.001
	D	18.25	5.75786	0.018
	A	-47.375	5.75786	< 0.001
B	C	-8.625	5.75786	0.452
	D	-29.125	5.75786	< 0.001
	A	-3,876,000	5.75786	< 0.001
C	B	8.625	5.75786	0.452
	D	-20.5	5.75786	0.007
	A	-18.25	5.75786	0.018
D	B	29.125	5.75786	< 0.001
	C	20.5	5.75786	0.007

Table – III: Chi-Square test showing comparison of frequencies and percentages of the histological parameters among different groups

Histological Parameters		Group "A"		Group "B"		Group "C"		Group "D"		Total	
		N	%	N	%	N	%	N	%	N	%
Central Vein Congestion Hepatic Lobular Pattern	Absent	6	75	0	0	0	0	6	75	12	37.5
	Present	2	25	8	100	8	100	2	25	20	62.5
	Total	8	100	8	100	8	100	8	100	32	100
	Irregular	0	0	6	75	5	62.5	1	12.5	12	37.5
	Regular	8	100	2	25	3	37.5	7	87.5	20	62.5
	Total	8	100	8	100	8	100	8	100	32	100
Periportal Inflammation	Absent	5	62.5	0	0	0	0	1	12.5	6	18.8
	Mild	3	37.5	0	0	0	0	7	87.5	10	31.2
	Moderate	0	0	1	12.5	3	37.5	0	0	4	12.5
	Severe	0	0	7	87.5	5	62.5	0	0	12	37.5
	Total	8	100	8	100	8	100	8	100	32	100
Hepatocyte Vacuolation	Absent	6	75	0	0	0	0	3	37.5	9	28.1
	Mild	2	25	0	0	0	0	4	50	6	18.8
	Moderate	0	0	0	0	0	0	1	12.5	1	3.1
	Severe	0	0	4	50	6	75	0	0	10	31.2
	Very Severe	0	0	4	50	2	25	0	0	6	18.8
	Total	8	100	8	100	8	100	8	100	32	100



DISCUSSION:

This research was performed to determine flaxseed oil effect on hepatic injury due to Lipofundin intravenous injections in adult albino male rats. The groups C & D demonstrated rise in weight but decreased gain in weight than "A" group; whereas, decrease in weight was observed in "B" group. Previously, weight gain was observed which showed that (dietary flaxseed oil) is a cause of clear weight gain than (control group) due to high lipid content presence [10].

Because of type of (lipid content) present, another research found that groups treated with flaxseed oil showed rise in weight as compared to control group. The factor responsible for change in weight was (polyunsaturated fatty acids) present in flaxseed diet [12]. To ass's effects of flaxseed oil & Lipofundin, (histological check-up of the hepatic tissue) was carried out.

There was clear change in (hepatic lobular pattern) in various groups. This pattern was observed normal in groups treated with flaxseed oil serving as control. Distortion in lobular pattern was due to (intravenous infusion) of Lipofundin. The oxidative stress in hepatocytes is due to Lipofundin leading to central venous congestion & distorted (lobular pattern). The distortion was soon controlled when dealt using (flaxseed oil) after the treatment with Lipofundin in group D as in table 1.

Due to its antioxidant & anti-inflammatory effect, flaxseed oil recovered it soon. After treating with (Lipofundin administration), the central vein demonstrated clear congestion. The congestion was clearly minimized when rats were given (flaxseed oil) after treating with Lipofundin.

In the group treated with Lipofundin, (periportal inflammatory cells) were enhanced in concentration & recovery was observed after (flaxseed oil management). Anti-inflammatory effect was

observed by flaxseed oil on wound due to Lipofundin.

For its inflammatory effects, (Lipofundin administration) was studied previously which were because of polyunsaturated fatty acids presence & arachidonic acid metabolites; which also enhance thromboxane's production with leukotrienes which is causing inflammation [3]. The individuals suffering from (intestinal failure), liver biopsy specimen demonstrated (periportal inflammatory infiltration) because of (Lipofundin administration) as a part of the (parenteral nutrition therapy) [18].

This is exactly what our present study shows as soya bean-based oil emulsions are always causing hepatic tissue injury. The flaxseed oil has omega - 3 oils & has shown same (anti-inflammatory effect) in this research. With anti-inflammatory properties, flaxseed has necessary fatty acids & lignin's. Due to hepatic vacuolation, the fat accumulation was observed in groups treated with Lipofundin & recovery was gained after the management of Lipofundin flaxseed oil).

Reduction of flaxseed oil was caused in (lipid accumulation) in hepatocytes. The groups treated with Lipofundin, basement membrane was observed disrupted & recovered when treating with flaxseed oil. It shows that hepatic injury is caused by Lipofundin & recovered when treated with flaxseed oil. It was found in a previous human-based research, periportal inflammation is caused by Lipofundin administration with steatosis in (liver biopsy specimen).
Fish oil instead of soya bean oil was given to liver biopsy patients showing steatosis & no inflammation which indicates that those oils which have omega - 3 are best for hepatocytes comparing with soya bean [19]. We have used flaxseed oil having omega - 3 fatty acids & assisted in amelioration in our present study.

This research proved that flaxseed oil has good effects in protecting hepatic tissue which was damaged by Lipofundin as it damaged hepatic tissue & recovered by treating with flaxseed oil. This oil has (phytoestrogen lignin's) & (polyunsaturated fatty acids) which are causing anti-oxidant & anti-inflammatory properties. All these properties assisted in recovery process of (hepatic tissue damage) because of Lipofundin.

CONCLUSION:

Hepatic tissue damage is caused by (Lipofundin Flaxseed oil) & Lipofundin. The flaxseed oil has an ameliorative effect on it. So by using it, we may avoid hepatic tissue damage which is caused by (Lipofundin) and is used for (parenteral therapies).

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