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EVALUATING HYPOLIPIDEMIC POTENTIAL OF KASNI SEED (*CICHORIUM INTYBUS*) PREPARATIONS IN NEWLY DIAGNOSED PATIENTS OF METABOLIC DISORDER

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ABSTRACT: Objective: To evaluate hypolipidemic potential of Kasni (*Cichorium intybus*) seed preparations combined with oral hypoglycemic agent in treatment of patients of newly diagnosed type 2 DM. **Methods:** Newly diagnosed 90 patients of Type2DM, age 35-65years, of either sex were divided into 3 groups. Each group having 30 patients (19 male and 11 females) matched with each other in terms of age and sex. In group I only Glycomet SR once a day and in group II/III 6 grams crude seed powder or 50 ml decoction of crude seed powder twice a day in combination with Glycomet SR once in a day, was given for 90 days. Serum cholesterol, triglyceride, LDL and HDL levels were measured at zero, 30th, 60th and 90th day. **Results:** All the three groups showed a significant reduction in cholesterol, triglyceride and LDL across the four time periods. Post hoc Tukey HSD test shown that there was a significant difference between group I & II (p=0.045) and group I & III (p=0.000) for cholesterol; group I & II (p=0.008) and group I & III (p=0.000) for triglyceride and I & II (p=0.032) and group I & III (p=0.001) for LDL. While there was a significant increase found in HDL level. **Conclusions:** The add on therapy with Kasni seed preparations is more effective as hypolipidemic agent than only oral hypoglycaemic agent in decreasing serum cholesterol, triglyceride and LDL levels of selected patients. Among Kasni seed preparation treated groups, decoction was found better than crude seed powder.

INTRODUCTION: The metabolic disorders are main and increasing public-health and clinical challenge worldwide because of urbanization, excessive energy intake, increasing obesity, and sedentary life styles [1]. According to International Diabetes Federation (IFD) diabetes is one of the major metabolic disorders and a dangerous risk factor for heart problems. Twenty five percent of the world's adults have metabolic disorders [2]. Recently in year 2013 the American Heart Association also reported that adults (age 20 or above) have abnormal serum lipid profile [3].

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Persons with such conditions are twice as likely to die from, and thrice as likely to have a heart attack or stroke as compared with others. Type 2 diabetes mellitus is one of the most common chronic diseases in the whole world and the fourth or fifth leading cause of death in the developed countries; it accounts for 90 percent of all diabetes and has become one of the major causes of premature ill health and death - mainly through the increased risk of cardiovascular disease (CVD) which is responsible for up to 80 percent of these deaths. As per a projection, there will be about 23.3 million deaths by CVD worldwide by 2030 [4].

However, even before levels of blood glucose are high enough for a person to be diagnosed with diabetes, hyperglycaemia and related changes in blood lipids (hypertriglyceridemia, hypercholesterolemia and decrease in the 'good' cholesterol HDL-c increase a person's risk of CVD

[2]. Diabetes like metabolic disorder and hyperlipidemia has strong correlation with each other and are considered as a first order risk factor for atherothrombotic complications.

Worldwide, the first curative line of metabolic disorder was non-pharmacologic actions consisted of diet and lifestyle changes as well as appropriate care in order to decrease mortality and morbidity of such diseases. However, the major concern for medical scientists to find pharmacologic approach, and to increase the efficacy of chronic drug treatment. Medical researchers do have tendency to find curative agents among traditional sources [5]. As per World Health Organization (WHO) about 70 percent population of entire world depends upon traditional and folk medicines. In India, about 80 percent of the rural population depends upon traditional and folk medicines for their health care [6]. In this respect, many plant extracts have been assessed for their efficacy in metabolic disorders and hyperlipidemia; the Kasni (*Cichorium intybus*) is one of them, having a long history of therapeutic use in traditional medicine for many diseases specially diabetes [5, 7, 8].

The genus *Cichorium* (Asteraceae) is made of six species with main distribution areas in Europe and Asia; *Cichorium intybus* L., commonly known as Chicory or Kasni is a medicinally important plant [9, 10]. Therefore, present study is one of initial attempt to investigate the beneficial effect of Kasni seeds in combination with oral hypoglycemic agents in treatment of patients with newly diagnosed metabolic disorder i.e. type 2 diabetes mellitus with regard to its hypolipidemic potential because IDF has also recommended to lower cholesterol and trigyceride, raise HDL and reduce LDL in diabetes.

MATERIAL AND METHODS:

In the present study, 90 patients of either sex, with newly diagnosed type 2 diabetes mellitus, age ranging between 35 to 65 years were included. All included patients were free from diabetic complications like CVD/ IHD, Neuropathy, Nephropathy and Retinopathy or any other disease. Pregnant and lactating women were not included in the study. The study was conducted in one of the most reputed medical institutions of India i.e. OPD of Medicine department, King George's Medical University, Lucknow, India during 1st March 2013 to 30th May, 2013. There were 19 males and 11 females in each group i.e. total 57 male and 33 female patients were selected for the present study. The study protocol was approved by Institutional Ethics Committee, King George's Medical University, Lucknow, U.P., India (Ref.Code: 58 E.C.M. IIB/P21, letter no.: 2649/R.Cell 12 dated 20.10.2012). All participants were provided with specific written information about the aims of the study according to the Declaration of Helsinki, before their written consents were taken.

The selected participants were informed about all possible expected outcomes from the study. Written consent was taken from the study subjects. The included ninety (90) patients were divided into 3 groups. Each group having 30 patients (19 male and 11 females)(n=30) matched with each other in terms of age and sex.. The group - I patients on oral hypoglycemic agent were advised not to take any herbo-mineral preparation during the study duration, and this group served as standard. The patients of group – II were advised with Kasni crude seed powder (6 gms in the morning in fasting condition and 6 gms in the evening) in combination to oral hypoglycemic agent. The patients of group – III were advised with Kasni decoction (by instructing the patients to boil provided 6 grams crude seed powder in 100 ml water till 50 ml decoction remained) in combination to oral hypoglycemic agent.

The oral hypoglycemic agent prescribed was Glycomet SR containing Metformin Sustained Release once in a day in every group for 90 days. Preparations of Kasni seeds were given twice everyday upto 90 days in group II and III. A supervisor cautiously ensured that the selected patients were taking preparations of Kasni seeds appropriately. Blood samples were collected from all subjects before starting oral hypoglycemic agent/combination of crude *Cichorium intybus* seed powder and hypoglycemic agent/combination of *Cichorium intybus* crude seed powder decoction and oral hypoglycemic agent. Final sample was collected 12 hours after the last dose of 90th day treatment with standard drug and in combination with preparations of Kasni seeds.

Plant material collection and Authentication:
Indigenous variety of Kasni seeds were obtained from International Institute of Herbal Medicine, Lucknow, through Organic India Pvt. Ltd. from organic certified fields. It carries WHO standard for identification of herbs. Some of these seeds were cultivated in the herbal garden of C.S.J.M. University, Kanpur and then grown plant was supplied to National Botanical Research Institute (NBRI) Lucknow, India, there it was identified as *Cichorium intybus* L. (Ref. No: NBRI/CIF/222/2011).

The seeds of Kasni were cleaned, desiccated and crushed to a powder with an electric microniser. The envelopes containing 6 gms of Kasni seed powder were prepared and provided to patients of group II and group III with respective instructions i.e. to take as such crude seed powder (preparation 1) for group II or by preparing infusion by boiling in group III (preparation 2), and patients were asked to use it regularly as per direction. Advices about dietary and lifestyle changes were given to both Kasni treated groups and standard group.

Biochemical Analysis of Serum Parameters:
Each patient's lipid profile was measured by recording fasting blood sample, at the beginning of the trial (zero day), then at 30th, 60th, and 90 days. Venous blood sample was collected in plain tube clot activator vacutainer from each subject for the serum cholesterol, triglyceride, LDL & HDL levels estimation. All biochemical serum analysis was performed with fully automatic random access analyzer Biosystem A-25 manufactured by Biosystem Diagnostics Pvt. Ltd. an ISO 9001:13485 standard and CE mark company. The consent was obtained from the patients and blood samples were taken after an overnight fast at baseline and during three months of the study. Serum Cholesterol/triglyceride/LDL and HDL values were measured by using the oxidase/peroxidase method and expressed in mg/dl.

Statistical Analysis:
Statistical analyses were conducted on IBM SPSS Version 20 software by using mixed between-within subjects ANOVA followed by post Hoc Tukey HSD test to make a comparison between groups. Results are presented as mean ± SD. *P* - values < 0·05 were considered statistically significant.

RESULTS:
A mixed between- within subjects analysis of variance was conducted to compare the effects of three types of treatments (Group I, II & III) on Serum cholesterol, triglyceride, LDL and HDL levels across four time periods (zero day, 30th day, 60th day, and 90th day).

Serum Cholesterol:
There was a significant interaction between time and type of treatments, Wilk's Lambda=0.252, F(6, 170)=28.070, p<0.001, partial eta squared=0.498 (**Table 1**).

TABLE 1: INTERACTION BETWEEN TIME AND TYPE OF TREATMENTS AND MAIN EFFECT FOR TIME
Measure- Cholesterol
Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
T	Pillai's Trace	.990	2672.105[b]	3.000	85.000	.000	.990
	Wilks' Lambda	.010	2672.105[b]	3.000	85.000	.000	.990
	Hotelling's Trace	94.310	2672.105[b]	3.000	85.000	.000	.990
	Roy's Largest Root	94.310	2672.105[b]	3.000	85.000	.000	.990
T * GROUP	Pillai's Trace	.807	19.380	6.000	172.000	.000	.403
	Wilks' Lambda	.252	28.070[b]	6.000	170.000	.000	.498
	Hotelling's Trace	2.729	38.204	6.000	168.000	.000	.577
	Roy's Largest Root	2.640	75.687[c]	3.000	86.000	.000	.725

a. Design: Intercept + GROUP

Within Subjects Design: T

b. Exact statistic

c. The statistic is an upper bound on F that yields a lower bound on the significance level.

There was a significant main effect for time, Wilk's Lambda=0.010, F(3, 85)=2672.105, p<0.001, partial eta squared=0.990 (**Table 1**), with all groups showing a reduction in Serum Cholesterol level across the four time periods (**Table 2).**

TABLE 2: SERUM CHOLESTEROL LEVEL (mg/dl) FOR ALL THE THREE GROUPS ACROSS FOUR TIME PERIODS

	Group I (Only oral Hypoglycemic agent used)			Group II (Kasni crude seed powder & Oral Hypoglycemic agent used)			Group III (Decoction of Kasni seed powder & Oral Hypoglycemic agent used)		
Time Periods	**M**	**SD**	**N**	**M**	**SD**	**N**	**M**	**SD**	**N**
1. Zero day	215.9000	6.05350	30	215.2333	8.12694	30	213.5333	8.26598	30
2. Thirty days	207.6000	6.25107	30	201.7667	8.24489	30	198.6333	8.07928	30
3. Sixty days	203.5000	6.33409	30	198.2667	7.25370	30	193.9000	7.26043	30
4. Ninety days	197.4667	5.06328	30	191.6333	6.89569	30	187.6333	6.98019	30

The main effect comparing the three type of treatments was significant, F(2,87)=9.088, p=0.000 (p<.05), partial eta squared=0.173, suggesting large difference in the effectiveness of the three treatments (**Table 3**).

TABLE 3: ANALYSIS OF BETWEEN GROUP EFFECTS

Measure: Cholesterol
Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	14702370.844	1	14702370.844	74776.975	.000	.999
GROUP	3573.539	2	1786.769	9.088	.000	.173
Error	17105.617	87	196.616			

Post hoc Tukey HSD test is showing that there is a significant difference between Group I & II (p=0.045) and Group I & III (p=0.000) (**Table 4**). So, Kasni crude seed powder with oral hypoglycaemic agent and Kasni seed powder decoction with oral hypoglycaemic agent is more effective than only oral hypoglycaemic agent in decreasing Serum Cholesterol level of selected patients.

TABLE 4: MULTIPLE COMPARISONS GROUP I, II & III FOR SERUM CHOLESTEROL LEVEL

Measure: Cholesterol

	(I) GROUP	(J) GROUP	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	A	B	4.3917*	1.81023	.045	.0752	8.7081
		C	7.6917*	1.81023	.000	3.3752	12.0081
	B	A	-4.3917*	1.81023	.045	-8.7081	-.0752
		C	3.3000	1.81023	.168	-1.0165	7.6165
	C	A	-7.6917*	1.81023	.000	-12.0081	-3.3752
		B	-3.3000	1.81023	.168	-7.6165	1.0165

Based on observed means.
The error term is Mean Square (Error) = 49.154.
*. The mean difference is significant at the .05 level.

Profile plot is showing Kasni seed powder decoction with oral hypoglycaemic agent is more effective than Kasni crude seed powder with oral hypoglycaemic agent in decreasing serum cholesterol level (**Fig. 1**).

Serum Triglyceride:

There was a significant interaction between time and type of treatments, Wilk's Lambda=0.173, F(6, 170)=39.882, p<0.001, partial eta squared=0.585 (**Table 5)**

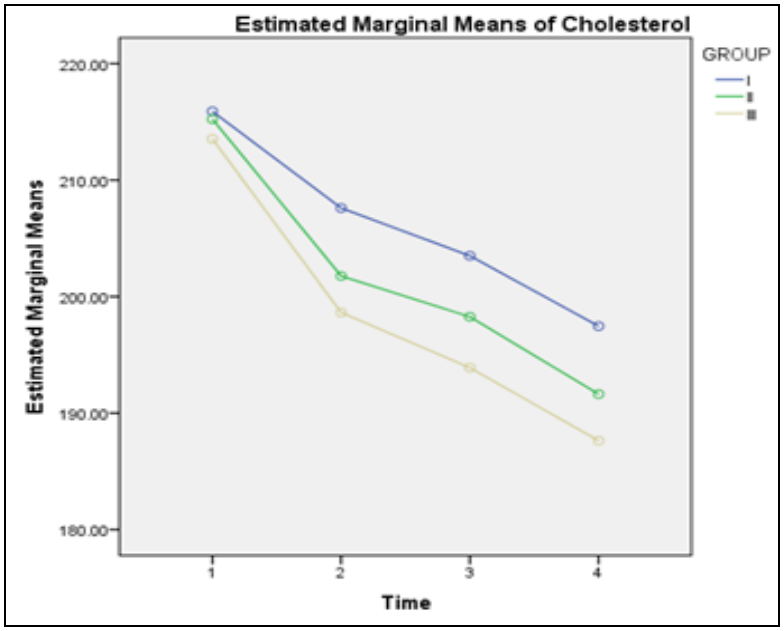

FIG. 1: COMPARATIVE ANALYSIS OF GROUP I, II & III FOR SERUM CHOLESTEROL LEVEL

TABLE 5: INTERACTION BETWEEN TIME AND TYPE OF TREATMENTS AND MAIN EFFECT FOR TIME

Measure- Trigyceride

Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
TIME	Pillai's Trace	.986	2070.203[b]	3.000	85.000	.000	.986
	Wilks' Lambda	.014	2070.203[b]	3.000	85.000	.000	.986
	Hotelling's Trace	73.066	2070.203[b]	3.000	85.000	.000	.986
	Roy's Largest Root	73.066	2070.203[b]	3.000	85.000	.000	.986
TIME * GROUP	Pillai's Trace	.832	20.432	6.000	172.000	.000	.416
	Wilks' Lambda	.173	39.882[b]	6.000	170.000	.000	.585
	Hotelling's Trace	4.769	66.762	6.000	168.000	.000	.705
	Roy's Largest Root	4.763	136.536[c]	3.000	86.000	.000	.826

a. Design: Intercept + GROUP
Within Subjects Design: TIME

b. Exact statistic

c. The statistic is an upper bound on F that yields a lower bound on the significance level.

There was a significant main effect for time, Wilk's Lambda=0.014, F(3, 85)=2070.203, p<0.001, partial eta squared=0.986 (**Table 5**), with all groups showing a reduction in Serum Triglyceride level across the four time periods (**Table 6).**

TABLE 6: TRIGLYCERIDE LEVEL (mg/dl) FOR ALL THE THREE GROUPS ACROSS FOUR TIME PERIODS

	Group I (Only oral Hypoglycemic agent used)			Group II (Kasni crude seed powder & Oral Hypoglycemic agent used)			Group III (Decoction of Kasni seed powder & Oral Hypoglycemic agent used)		
Time Periods	**M**	**SD**	**N**	**M**	**SD**	**N**	**M**	**SD**	**N**
1. Zero day	145.6333	6.65652	30	144.5000	7.22901	30	143.2000	10.14855	30
2. Thirty days	139.3000	6.24307	30	133.0000	6.35718	30	129.3000	10.35624	30
3. Sixty days	135.4667	5.96966	30	128.3000	5.60265	30	124.5667	9.90536	30
4. Ninety days	128.9333	6.29139	30	119.7667	5.07654	30	114.9333	8.91699	30

The main effect comparing the three type of treatments was significant, F(2,87)=11.904, p=0.000 (p<.05), partial eta squared=0.215, suggesting large difference in the effectiveness of the three treatments (**Table 7**).

TABLE 7: ANALYSIS OF BETWEEN GROUP EFFECTS

Measure: Triglyceride
Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	6295629.025	1	6295629.025	27979.847	.000	.997
GROUP	5356.717	2	2678.358	11.904	.000	.215
Error	19575.508	87	225.006			

Post hoc Tukey HSD test is showing that there is a significant difference between Group I & II (p=0.008) and Group I & C (p=0.000) (**Table 8**.) So Kasni crude seed powder with oral hypoglycaemic agent and Kasni seed powder decoction with oral hypoglycaemic agent is more effective than only oral hypoglycaemic agent in decreasing Serum Triglyceride level of selected patients.

TABLE 8: MULTIPLE COMPARISONS GROUP I, II & III FOR TRIGLYCERIDE LEVEL

Measure: TRIGYCERIDE

	(I) GROUP	(J) GROUP	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	A	B	5.9417*	1.93652	.008	1.3241	10.5593
		C	9.3333*	1.93652	.000	4.7157	13.9509
	B	A	-5.9417*	1.93652	.008	-10.5593	-1.3241
		C	3.3917	1.93652	.192	-1.2259	8.0093
	C	A	-9.3333*	1.93652	.000	-13.9509	-4.7157
		B	-3.3917	1.93652	.192	-8.0093	1.2259

Based on observed means.
The error term is Mean Square(Error) = 56.251.
*. The mean difference is significant at the .05 level.

Profile plot is showing Kasni seed powder decoction with oral hypoglycaemic agent is more effective than Kasni crude seed powder with oral hypoglycaemic agent in decreasing serum triglyceride level. (**Fig.2**)

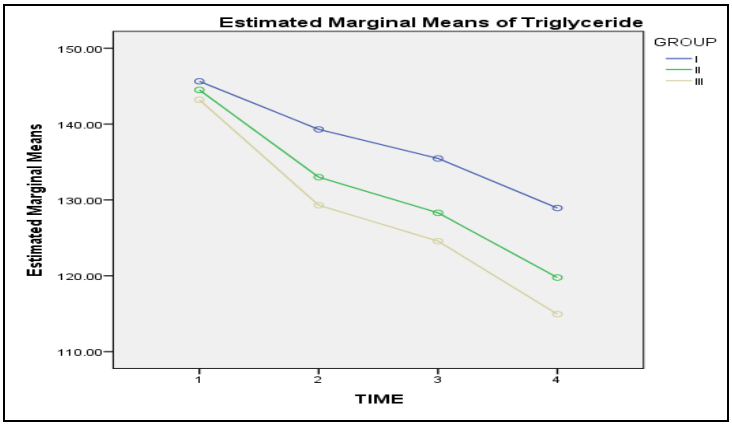

FIG. 2: COMPARATIVE ANALYSIS OF GROUP I, II & III FOR TRIGLYCERIDE LEVEL

Serum LDL:

There was a significant interaction between time and type of treatments, Wilk's Lambda=0.298, F(6, 170)=23.599, p<0.001, partial eta squared=0.454 (**Table 9**).

TABLE 9: INTERACTION BETWEEN TIME AND TYPE OF TREATMENTS AND MAIN EFFECT FOR TIME

Measure- LDL

Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
Time	Pillai's Trace	.978	1279.327[b]	3.000	85.000	.000	.978
	Wilks' Lambda	.022	1279.327[b]	3.000	85.000	.000	.978
	Hotelling's Trace	45.153	1279.327[b]	3.000	85.000	.000	.978
	Roy's Largest Root	45.153	1279.327[b]	3.000	85.000	.000	.978
Time * Group	Pillai's Trace	.742	16.922	6.000	172.000	.000	.371
	Wilks' Lambda	.298	23.599[b]	6.000	170.000	.000	.454
	Hotelling's Trace	2.225	31.149	6.000	168.000	.000	.527
	Roy's Largest Root	2.163	61.999[c]	3.000	86.000	.000	.684

a. Design: Intercept + GROUP
Within Subjects Design: TIME

b. Exact statistic

c. The statistic is an upper bound on F that yields a lower bound on the significance level.

There was a significant main effect for time, Wilk's Lambda=0.022, F(3, 85)=1279.327, p<0.001, partial eta squared=0.978 (**Table 9**), with all groups showing a reduction in Serum LDL level across the four time periods (**Table 10**).

TABLE 10: SERUM LDL LEVEL (mg/dl) FOR ALL THE THREE GROUPS ACROSS FOUR TIME PERIODS

	Group I (Only oral Hypoglycemic agent used)			Group II (Kasni crude seed powder & Oral Hypoglycemic agent used)			Group III (Decoction of Kasni seed powder & Oral Hypoglycemic agent used)		
Time Periods	M	SD	N	M	SD	N	M	SD	N
1. Zero day	132.0333	7.14135	30	131.0000	6.14200	30	129.7000	7.67059	30
2. Thirty days	127.7333	7.01689	30	122.8000	5.65929	30	120.6667	8.17622	30
3. Sixty days	125.1667	6.92862	30	119.3333	5.60993	30	116.2000	8.20597	30
4. Ninety days	119.8333	7.15871	30	113.3667	5.23571	30	110.2667	7.95216	30

The main effect comparing the three type of treatments was significant, F(2,87)=7.947, p=0.001 (p<.05), partial eta squared=0.154, suggesting large difference in the effectiveness of the three treatments (**Table 11**).

TABLE 11: ANALYSIS OF BETWEEN GROUP EFFECTS

Measure: LDL

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	5388294.025	1	5388294.025	28371.872	.000	.997
GROUP	3018.467	2	1509.233	7.947	.001	.154
Error	16522.758	87	189.917			

Post hoc Tukey HSD test is showing that there is a significant difference between Group I & II (p=0.032) and Group I & C (p=0.001) (**Table 12**). So, Kasni crude seed powder with oral hypoglycaemic agent and Kasni seed powder decoction with oral hypoglycaemic agent is more effective than only oral hypoglycaemic agent in decreasing serum LDL level of selected patients.

TABLE 12: MULTIPLE COMPARISONS GROUP I, II & III FOR SERUM LDL LEVEL

Multiple Comparisons

Measure: LDL

	(I) GROUP	(J) GROUP	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	A	B	4.5667*	1.77912	.032	.3244	8.8089
		C	6.9833*	1.77912	.001	2.7411	11.2256

	B	A	-4.5667*	1.77912	.032	-8.8089	-.3244
		C	2.4167	1.77912	.367	-1.8256	6.6589
	C	A	-6.9833*	1.77912	.001	-11.2256	-2.7411
		B	-2.4167	1.77912	.367	-6.6589	1.8256

Based on observed means.
The error term is Mean Square (Error) = 47.479.
*. The mean difference is significant at the .05 level.

Profile plot is showing Kasni seed powder decoction with oral hypoglycaemic agent is more effective than Kasni crude seed powder with oral hypoglycaemic agent in decreasing serum LDL level. **(Fig. 3)**

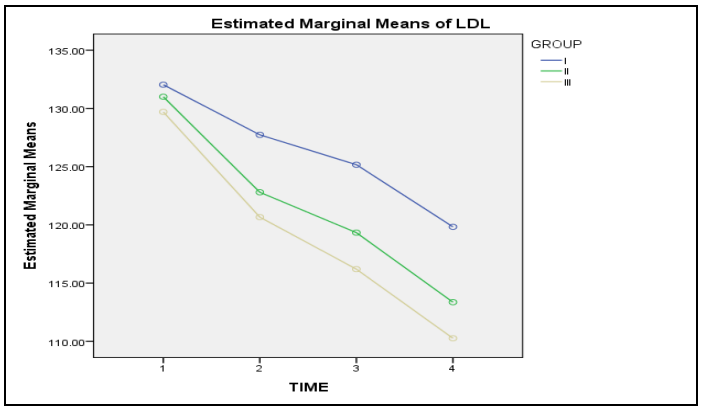

FIG. 3: COMPARATIVE ANALYSIS OF GROUP I, II & III FOR SERUM LDL LEVEL

Serum HDL:

There was a significant interaction between time and type of treatments, Wilk's Lambda=0.111, F (6, 170) =56.575, p<0.001, partial eta squared=0.666 (**Table 13**).

TABLE 13: INTERACTION BETWEEN TIME AND TYPE OF TREATMENTS AND MAIN EFFECT FOR TIME

Measure: HDL
Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
TIME	Pillai's Trace	.988	2299.902[b]	3.000	85.000	.000	.988
	Wilks' Lambda	.012	2299.902[b]	3.000	85.000	.000	.988
	Hotelling's Trace	81.173	2299.902[b]	3.000	85.000	.000	.988
	Roy's Largest Root	81.173	2299.902[b]	3.000	85.000	.000	.988
TIME * GROUP	Pillai's Trace	.924	24.635	6.000	172.000	.000	.462
	Wilks' Lambda	.111	56.575[b]	6.000	170.000	.000	.666
	Hotelling's Trace	7.660	107.236	6.000	168.000	.000	.793
	Roy's Largest Root	7.618	218.372[c]	3.000	86.000	.000	.884

a. Design: Intercept + GROUP
Within Subjects Design: TIME
b. Exact statistic
c. The statistic is an upper bound on F that yields a lower bound on the significance level.

There was a significant main effect for time, Wilk's Lambda=0.012, F(3, 85)=2299.902, p<0.001, partial eta squared=0.988 (**Table 13**), with all groups showing an increasing in Serum HDL level across the four time periods. (**Table 14)**

TABLE 14: SERU HDL LEVEL (mg/dl) FOR ALL THE THREE GROUPS ACROSS FOUR TIME PERIODS

	Group I (Only oral Hypoglycemic agent used)			Group II (Kasni crude seed powder & Oral Hypoglycemic agent used)			Group III (Decoction of Kasni seed powder & Oral Hypoglycemic agent used)		
Time Periods	**M**	**SD**	**N**	**M**	**SD**	**N**	**M**	**SD**	**N**
1. Zero day	42.7000	2.58844	30	43.0000	4.22635	30	44.1333	4.91116	30

2.	Thirty days	44.6000	2.59442	30	47.3000	4.06965	30	48.8667	4.75419	30
3.	Sixty days	45.4000	2.41547	30	48.6000	3.91813	30	50.0000	4.83522	30
4.	Ninety days	46.7333	2.47656	30	50.7333	3.90343	30	52.0667	4.80613	30

The main effect comparing the three type of treatments was significant, F(2,87)=7.805, p=0.001 (p<.05), partial eta squared=0.152, suggesting large difference in the effectiveness of the three treatments (**Table 15**).

TABLE 15: ANALYSIS OF BETWEEN GROUP EFFECTS

Measure: HDL
Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	795616.044	1	795616.044	13143.063	.000	.993
GROUP	944.906	2	472.453	7.805	.001	.152
Error	5266.550	87	60.535			

Post hoc Tukey HSD test is showing that there is a significant difference between Group I & II (p=0.034) and Group I & C (p=0.001) (**Table 16**). So, Kasni crude seed powder with oral hypoglycaemic agent and Kasni seed powder decoction with oral hypoglycaemic agent is more effective than only oral hypoglycaemic agent in increasing Serum HDL level of selected patients.

TABLE 16: MULTIPLE COMPARISONS GROUP I, II & III FOR SERUM HDL LEVEL

Measure: HDL

	(I) GROUP	(J) GROUP	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	A	B	-2.5500*	1.00445	.034	-4.9451	-.1549
		C	-3.9083*	1.00445	.001	-6.3034	-1.5132
	B	A	2.5500*	1.00445	.034	.1549	4.9451
		C	-1.3583	1.00445	.370	-3.7534	1.0368
	C	A	3.9083*	1.00445	.001	1.5132	6.3034
		B	1.3583	1.00445	.370	-1.0368	3.7534

Based on observed means.
The error term is Mean Square(Error) = 15.134.
*. The mean difference is significant at the .05 level.

Profile plot is showing Kasni seed preparations are effective in increasing serum HDL level (**Fig.4).**

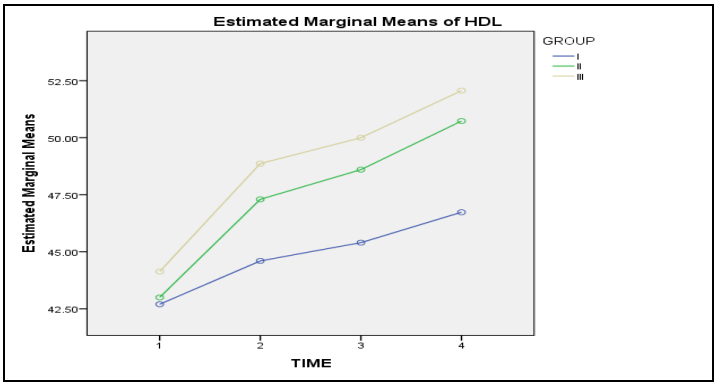

FIG. 4: COMPARATIVE ANALYSIS OF GROUP I, II & III FOR SERUM HDL LEVEL

DISCUSSION: Adverse effects, cost factor and part of patients' intolerance to the pharmacotherapy with western medicine make traditional herbal medicine one of their alternatives and this is one of the initial attempts for evaluating the effect of traditional herbal medicinal Kasni seeds on lipid profile of newly diagnosed diabetes mellitus type 2 patients. Results obtained in the present study shown that reduction in serum cholesterol level of selected patients were more (P<0.05) in *C. intybus* treated group II (11%) and III (12%) as compared to standard group I (9%); reduction in serum

triglyceride were more (P<0.05) in *C. intybus* treated group II (17%) and III (20%) as compared to standard group I (11%) and reduction in serum LDL level of selected patients were also more (P<0.05) in *C. intybus* treated group II (13%) and III (15%) as compared to standard group I (9%).

While serum HDL level of selected patients was increased in group II (17.984%) and III (17.976%) as compared to standard group I (9%). Significant improvement in serum HDL level indicates that Kasni seeds can be used as add on therapy to those patients whose lipid control cannot be achieved by conventional drugs. Combinations of oral hypoglycemic drugs are used to achieve glycemic control and to improve hyperlipidemia due to hyperglycemia. Hypoglycemic drug Metformin (Glycomet SR), a biguanide agent, was used for this study. With the labeling of tolbutamide by the U.S. Food and Drug Administration in 1962, sulfonylurea class of drugs quickly became the mainstay of treatment for type 2 diabetes mellitus. But now newer agents have entered the marketplace, sulfonylurea drugs no more play a primary role in pharmacologic management of type 2 diabetes mellitus [11]. About two third patients of diabetes mellitus, who begin therapy with a sulfonylurea respond, although up to 20 percent of them require additional medication [12].

Glycomet SR (Metformin) was the drug of choice because of certain advantages like it lowers blood glucose mainly by decreasing hepatic glucose output and reducing insulin resistance and when used as monotherapy, Metformin does not cause hypoglycemia. The reported incidence of lactic acidosis during Metformin treatment is less than 0.1 cases per thousand patient years and the mortality risk is even lower. Metformin does not promote weight gain and can reduce plasma triglycerides by 15–20% and is the only drug that has been verified to reduce macrovascular events in type 2 diabetes mellitus [13].

Though, newly diagnosed patients of type 2 DM who were suffering from hyperlipidemia were screened out, even the hypolipidemic effect of chicory on lipid profile may be due to its main active compounds, like inulin which can cause alteration of hormone secretion which affect lipid metabolism. In accordance with the present results, Yassin and El-Hadidy [14] reported that chicory extract improved lipid profile by decreasing plasma total cholesterol and triglyceride values. These results were in agreement with those reported by Eman G. Helal et al.[15] who reported the hyperlipidemic effect of oxytetracycline was ameliorated with the treatment of rats with aqueous extract of chicory roots. The various other mechanisms proposed for the hypolipidemic activity of Kasni (*Cichorium intybus)*: Rub RA et al.[16] found that there was a significant decrease in serum triglycerides, total cholesterol levels and significant increase in serum HDL level in diabetic rats by *Cichorium intybus* polyphenol rich fraction (30mg/kg). Significant decrease in Serum LDL and alkaline phosphatase level were also reported but, there was no significant change in serum insulin.

It was attributed directly to its lipid decreasing activity or indirectly to its effect on various lipid regulation systems and concluded that the polyphenol rich fraction has extra pancreatic effects. Pushparaj et al.[17] induced diabetes by intraperitoneal injection of streptozotocin in male Sprague-Dawley rats against beta-cell damage and daily injection of ethanol extract of *Cichorium intybus* whole plant, at a dose of 125mg/Kg body weight for fourteen days, a marked decrease in the serum triglycerides and cholesterol was observed in the extract-treated rats. Hepatic glucose-6-phosphatase activity was found to be reduced in extract treated diabetic rats as compared to untreated diabetic rats. Ghamarian et al. [18] induced early-stage and late-stage diabetes in male Wistar albino rats by streptozotocin-niacinamide and streptozotocin alone, respectively. The treatment with aqueous *C. intybus* seed extracts produced decrease in triglyceride and total cholesterol in the blood of chicory-STZ rats in the early stage. The improved lipid metabolism and inhibition of adipogenesis were proposed for it. While in late-stage, the increase in total cholesterol over 28 days of exposure to chicory extract is due to an increase in HDL-cholesterol and chicory treatment also led to the increase in insulin levels pointing toward the insulin-sensitizing action of chicory. Asl et al .[5] had also supported that *Cichorium intybus* L. improves insulin sensitivity through inhibiting protein tyrosine phosphatase 1B (PTP1B) in adipogenic

insulin signaling cascade both *in vitro* and *in vivo*. Kaskoos RA[8] reported that aqueous extract of Kasni (*C. intybus*) seeds exhibited only moderate dose dependent hypolipidemic activity and atherogenic index in STZ-induced diabetic rats.

Atherogenic index was decreased more effectively and the increase in HDL was found to be higher. He ruled out the mechanism via intestinal delay or inhibition of glucose/lipid and any regeneration of pancreatic β cells but supported extra pancreatic mode of action and insulinotropic action of extract. Hardeep et al.[19] also found hypolipidemic action of methanolic extract of chicory roots in streptozocin induced diabetic rats. The effects of the standard drug (glibenclamide) on serum TG and cholesterol in the diabetic rats were comparable to those of the herbal extract. Reduction in serum levels of cholesterol and TG by administration of methanolic extract of chicory for 21 days was suspected by low activity of cholesterol biosynthesis enzymes and/or due to decrease in lipolysis which are under the control of insulin.

On the basis of present study authors suggests Kasni seed preparations as an adjuvant therapy to the newly diagnosed patients of uncomplicated type 2 diabetes mellitus. The use of Kasni seeds for primary prevention of dyslipidemia in patients with metabolic disorder could be promising after few more investigation of herb-drug interactions *in vivo* and clinically with major phytochemicals of Kasni (*C. intybus*).

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