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EVALUATING HYPOGLYCEMIC POTENTIAL OF KASNI (*CICHORIUM INTYBUS*) SEED PREPARATIONS IN TYPE 2 DIABETES MELLITUS PATIENTS

Praveen Katiyar [*1, 2], Amod Kumar [1], Arvind K. Mishra [3], Rakesh K. Dixit [1] and Ajay K. Gupta [4]

Department of Pharmacology & Therapeutics [1], Department of Internal Medicine [3], King George's Medical University, Lucknow, U.P., India.
University Institute of Health Sciences [2], University Institute of Pharmacy [4], C.S.J.M. University, Kanpur, U.P., India.

Keywords:

Hypoglycemia, Diabetes, Kasni, FBG, PPBG, HbA1c, Type2DM

Correspondence to Author:
Dr. Praveen Katiyar

Assistant Professor & Coordinator
University Institute of Health Sciences, C.S.J.M. University, Kanpur 208024, U.P., India.

E-mail: drpraveenkatiyar@gmail.com

ABSTRACT: Objective: To evaluate hypoglycemic responses of Kasni (*Cichorium intybus*) seed preparations in combination with oral hypoglycemic agent in treatment of patients of newly diagnosed type2DM. **Methods:** Newly diagnosed 90 patients of type2DM, age 35-65years, of either sex were divided into 3 groups. Each group had 30 patients (19 male and 11 females) matched with each other in terms of age and sex. In group A, only Glycomet SR once a day and in group B/C 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. FBG and PPBG were measured across 7 time periods and HbA1c levels were measured at zero and 90th day. **Results:** All the three groups shown a significant reduction in FBG and PPBG across the seven time periods. Post hoc TukeyHSD test shown that there was a significant difference between group A&B (p=0.027) and group A&C (p=0.000) for FBG and group A&B (p=0.019) and group A&C (p=0.000) for PPBG. Significant decrease in HbA1c levels was also found. Post hoc TukeyHSD test shown that there was a significant difference between group A&B (p=0.032) and group A&C (p=0.003) for HbA1c. **Conclusions:** The adjuvant therapy with Kasni seed preparations in newly diagnosed type2DM patients in combination with oral hypoglycaemic agent is more effective than only oral hypoglycaemic agent in decreasing FBG, PPBG & HbA1c of selected patients and among Kasni seed preparations treated groups, decoction was found better than crude seed powder.

INTRODUCTION: We are living in the era of transition in which the manual work has been shifted towards the machinery assistance. Along with this, there is a shift in life style and food habits. The sedentary life style and fast foods rich in calorie along with least manual work are some of the factors which predispose the present generation to develop lifestyle metabolic disorders including diabetes mellitus.

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Technological developments make our lifestyle sedentary and increase prevalence of chronic diseases like diabetes mellitus [1]. According to American Diabetes Association, Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels [2].

Diabetes, one of the most important chronic metabolic disorders, is associated with development of numerous significant complications in patients. These complications may be

macrovascular (coronary heart disease, peripheral vascular disease and stroke), microvascular (neuropathy, retinopathy and nephropathy) or both micro and macrovascular (diabetic foot) [3].

Diabetes has become one of the major concerns of Health Care Professionals because as per International Diabetes Federation Diabetes Atlas 6th Ed., 2014 update, by 2035 the estimated population suffering from diabetes mellitus will rise to 592 million. In year 2014, 387 million people in world had diabetes. The number of people with type 2 diabetes is increasing in every country. 77% of people with diabetes live in low and middle income countries. The greatest numbers of people with diabetes are between 40 and 59 years of age. 179 million people with diabetes are undiagnosed. Diabetes caused 4.9 million deaths in 2014; every seven seconds a person dies from diabetes. Diabetes caused at least USD 612 billion dollars in health expenditure in 2014 – 11% of total spending on adults [4].

Data of IDF Diabetes Atlas, 2014 update shows that, this disease is increasing very fast and there is a great need of more effective and economical treatment of diabetes.

Worldwide, the first therapeutic line of diabetes mellitus was non-pharmacologic measures consisted of diet and lifestyle modification as well as appropriate care in order to reduce mortality and morbidity of diabetes. 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 seek remedial agents among traditional sources [5]. According to World Health Organization (WHO) about 70% population of whole world rely upon traditional and folk medicines. In India, about 80% of the rural population depends upon traditional and folk medicines for their health care[6]. In this respect, lots of plant extracts have been assessed for their usefulness in diabetes mellitus and Kasni (*Cichorium intybus*) is one of them, which has a long history of therapeutic use in traditional medicine for various diseases particularly diabetes [5, 7, 8]. The genus *Cichorium* (Asteraceae) have six species with majorly distributed in Europe and Asia; *Cichorium intybus* L., popularly known as Kasni or chicory, is a medicinally important plant. This plant has immense medicinal importance because of the presence of various medicinally important compounds such as alkaloids, inulin, sesquiterpene lactones, coumarins, vitamins, chlorophyll pigments, unsaturated sterols, flavonoids, saponins and tannins [9]. Chicoric acid has been identified as the major compound, Aliphatic compounds and their derivatives comprise the main fraction while terpenoids comprise minor constituents of the plant. Octane, *n*-nonadecane, pentadecanone, hexadecane, methoxycoumarin cichorine, flavonoids, essential oils etc are the other constituents reported in Kasni [10].

Present study is one of the initial attempt to investigate the hypoglycemic effect of Kasni seed preparations in combination with oral hypoglycemic agent for treatment of patients with newly diagnosed diabetes mellitus type 2.

MATERIAL AND METHODS:

Present study was done on newly diagnosed patients of type 2 diabetes mellitus. A total of 90 patients of either sex, age ranging between 35 to 65 years, were selected from OPD of the Medicine Department, King George's Medical University, Lucknow, U.P., India. All included patients had no history of diabetic complications like CVD/IHD, Neuropathy, Nephropathy and Retinopathy or any other disease. Pregnant and lactating women were also excluded from the present study by taking detailed history and appropriate tests. The study was conducted during 1st March 2013 to 30th May, 2013.

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). According to the Declaration of Helsinki, all participants were provided with specific written information about the aims of the study before consents were obtained. The selected patients were informed about all possible expected advantages and disadvantages from the study. Informed consent from these patients was obtained before enrolling them under study.

The included ninety (90) patients were divided into 3 groups. Each group had 30 patients (19 male and 11 females) (n=30) matched with each other in terms of age and sex. In the group-A, 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 – B were advised with Kasni crude seed powder (Preparation-I, 6 gms in the morning in fasting condition and 6 gms in the evening) in combination to oral hypoglycemic agent. The patients of group – C were advised to take Kasni crude seed powder decoction (Preparation-II, 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 B and C. 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 Kasni crude seed powder and hypoglycemic agent/combination of Kasni 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: Kasni seeds of indigenous variety 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 plant grown was supplied to National Botanical Research Institute (NBRI) Lucknow, U.P., India. There it was identified as *Cichorium intybus* L. (Ref. No: NBRI/CIF/222/2011). The Kasni seeds were cleaned, desiccated and crushed to powder form with an electric microniser. The envelopes containing 6 gms of Kasni seed powder were prepared and provided to patients of group B and group C with respective instructions i.e. to take as such crude seed powder (preparation-I) by group B or by preparing infusion by boiling, in group C (preparation-II), and patients were asked to use it regularly as per direction. Advices about dietary and lifestyle changes were also given to both Kasni treated groups and standard group.

Biochemical Analysis:
Each patient's glycemic control was measured by recording fasting blood glucose (FBG), postprandial blood glucose (PPBG) at the beginning of the trial, then once every two weeks during the trial and HbA1c (glycated/glycosylated hemoglobin) at 0 and 90^{th} day. For fasting and postprandial blood glucose estimation, venous blood samples were collected in fluoride vacutainer and for HbA1c estimation venous blood samples were collected in the EDTA vacutainer.

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. Blood samples were taken after an overnight fast at baseline and during three months of the study. Fasting blood glucose and postprandial blood glucose were estimated by the Glucose Oxidase/Peroxidase method and expressed in mg/dl. HbA1c was assessed by immunoturbidimetric determination and expressed in percentage (%).

Statistical Analysis:
Statistical analysis 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 prepared as Mean$\pm$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 A, B & C) on fasting and postprandial blood glucose level across seven time periods (zero day, fifteen days, thirty days, forty five days, sixty days, seventy five days and ninety days).

Fasting blood glucose:

There was a significant interaction between time and type of treatments, Wilk's Lambda=0.257, F (12, 164) =13.294, p<0.001, partial eta squared=0.493 (**Table 1**).

TABLE 1: INTERACTION BETWEEN TIME AND TYPE OF TREATMENTS AND MAIN EFFECT FOR TIME

Measure – Fasting Glucose

Multivariate Tests[a]							
Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
Time	Pillai's Trace	.979	632.161[b]	6.000	82.000	.000	.979
	Wilks' Lambda	.021	632.161[b]	6.000	82.000	.000	.979
	Hotelling's Trace	46.256	632.161[b]	6.000	82.000	.000	.979
	Roy's Largest Root	46.256	632.161[b]	6.000	82.000	.000	.979
Time * Group	Pillai's Trace	.784	8.910	12.000	166.000	.000	.392
	Wilks' Lambda	.257	13.294[b]	12.000	164.000	.000	.493
	Hotelling's Trace	2.734	18.454	12.000	162.000	.000	.578
	Roy's Largest Root	2.675	37.005[c]	6.000	83.000	.000	.728

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=0.021, F (6, 82) =632.161, p<0.001, partial eta squared=0.979 (**Table 1),** with all groups showing a reduction in fasting blood glucose level across the seven time periods (**Table 2**).

TABLE 2: FASTING BLOOD GLUCOSE LEVEL (mg/dl) FOR ALL THE THREE GROUPS ACROSS SEVEN TIME PERIODS

		Group A (Only oral Hypoglycemic agent used)			Group B (Kasni crude seed powder & Oral Hypoglycemic agent used)			Group C (Decoction of Kasni seed powder & Oral Hypoglycemic agent used)		
	Time Periods	M	SD	N	M	SD	N	M	SD	N
1.	Zero day	140.9667	7.32254	30	140.8333	6.33590	30	141.1000	5.74366	30
2.	Fifteen day	136.7333	6.93285	30	133.4333	5.56270	30	130.7333	4.98227	30
3.	Thirty days	133.5333	6.69912	30	129.2000	4.64906	30	126.6667	4.58132	30
4.	Fourty Five days	129.4000	6.18452	30	126.1667	4.48048	30	123.9667	4.73056	30
5.	Sixty days	127.5333	5.89408	30	123.5333	4.44688	30	120.7333	4.66782	30
6.	Seventy Five days	124.5667	5.65492	30	120.1000	3.95971	30	116.7000	4.73541	30
7.	Ninety days	119.0667	4.86319	30	114.5667	3.24498	30	111.0667	3.57128	30

The main effect comparing the three type of treatments was significant, F (2, 87)=10.114, p=0.000, partial eta squared=0.189, suggesting large difference in the effectiveness of the three treatments (**Table 3**).

TABLE 3: ANALYSIS OF BETWEEN GROUP EFFECTS

Measure: Fasting Glucose

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	10188720.514	1	10188720.514	57110.436	.000	.998
Group	3608.924	2	1804.462	10.114	.000	.189
Error	15521.133	87	178.404			

Post hoc Tukey HSD test is showing that there is a significant difference between group A & B (p=0.027) and group A & C (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 fasting blood glucose level of selected patients.

TABLE 4: MULTIPLE COMPARISONS GROUP A, B & C FOR FASTING BLOOD GLUCOSE LEVEL

Measure: Fasting Glucose

	(I) GROUP	(J) GROUP	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	A	B	3.4238*	1.30349	.027	.3157	6.5320
		C	5.8333*	1.30349	.000	2.7252	8.9415
	B	A	-3.4238*	1.30349	.027	-6.5320	-.3157
		C	2.4095	1.30349	.160	-.6986	5.5177
	C	A	-5.8333*	1.30349	.000	-8.9415	-2.7252
		B	-2.4095	1.30349	.160	-5.5177	.6986

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

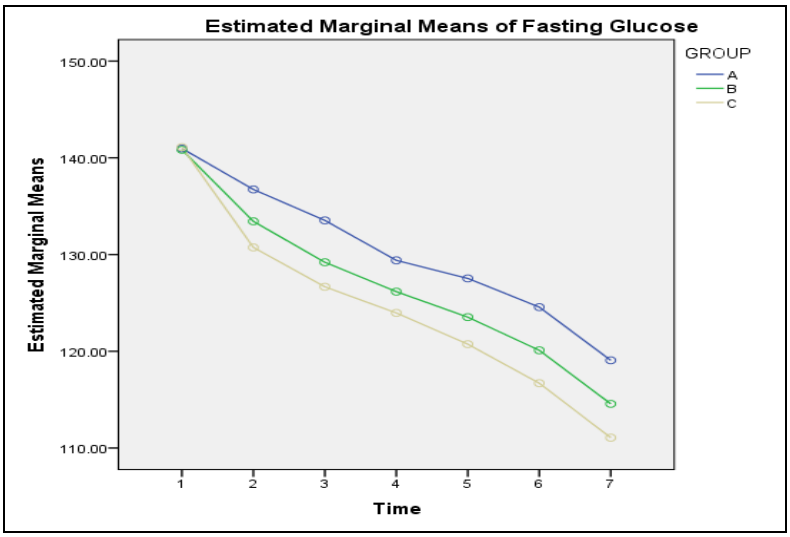

FIG. 1: COMPARATIVE ANALYSIS OF GROUP A, B & C FOR FASTING BLOOD GLUCOSE LEVEL

Postprandial blood glucose:

There was a significant interaction between time and type of treatments, Wilk's Lambda=0.552, F (12, 164) =4.724, p<0.001, partial eta squared=0.257 (**Table 5**).

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

Measure – Postprandial Glucose

Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
Time	Pillai's Trace	.979	651.361[b]	6.000	82.000	.000	.979
	Wilks' Lambda	.021	651.361[b]	6.000	82.000	.000	.979
	Hotelling's Trace	47.661	651.361[b]	6.000	82.000	.000	.979
	Roy's Largest Root	47.661	651.361[b]	6.000	82.000	.000	.979
Time * Group	Pillai's Trace	.479	4.361	12.000	166.000	.000	.240
	Wilks' Lambda	.552	4.724[b]	12.000	164.000	.000	.257
	Hotelling's Trace	.754	5.088	12.000	162.000	.000	.274
	Roy's Largest Root	.668	9.243[c]	6.000	83.000	.000	.401

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=0.021, F(6, 82)=651.361, p<0.001, partial eta squared=0.979 (**Table 5**), with all groups showing a reduction in post prandial blood glucose level across the seven time periods (Table 6).

TABLE 6: POSTPRANDIAL BLOOD GLUCOSE LEVEL (mg/dl) FOR ALL THE THREE GROUPS ACROSS SEVEN TIME PERIODS

	Group A (Only oral Hypoglycemic agent used)			Group B (Kasni crude seed powder & Oral Hypoglycemic agent used)			Group C (Decoction of Kasni seed powder & Oral Hypoglycemic agent used)		
Time Periods	**M**	**SD**	**N**	**M**	**SD**	**N**	**M**	**SD**	**N**
1. Zero day	196.8333	11.17288	30	194.1667	10.52447	30	196.2667	9.21742	30
2. Fifteen day	190.6000	9.69749	30	187.2000	8.09598	30	184.5667	8.42690	30
3. Thirty days	186.3667	8.46283	30	182.1667	7.62068	30	177.1000	6.57241	30
4. Fourty Five days	182.1667	7.80841	30	176.5333	7.57370	30	170.2333	6.07246	30
5. Sixty days	178.8667	7.45901	30	172.5333	7.09411	30	165.8667	5.43128	30
6. Seventy Five days	175.0333	6.82027	30	168.8000	6.74358	30	162.6000	5.44312	30
7. Ninety days	168.9667	6.53628	30	162.0667	6.03400	30	156.6000	5.58693	30

The main effect comparing the three type of treatments was significant, F (2,87)=13.095, p=0.000, partial eta squared=0.231, suggesting large difference in the effectiveness of the three treatments (**Table 7**).

TABLE 7: ANALYSIS OF BETWEEN GROUP EFFECTS
Measure: PP Glucose
Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	19934584.692	1	19934584.692	56500.296	.000	.998
Group	9240.308	2	4620.154	13.095	.000	.231
Error	30695.571	87	352.823			

Post hoc Tukey HSD test is showing that there is a significant difference between group A & B (p=0.019) and group A & 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 postprandial blood glucose level of selected patients.

TABLE 8: MULTIPLE COMPARISONS GROUP A, B & C FOR POSTPRANDIAL BLOOD GLUCOSE LEVEL
Measure: PP GLUCOSE

	(I) GROUP	(J) GROUP	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	A	B	5.0524*	1.83309	.019	.6814	9.4233
		C	9.3714*	1.83309	.000	5.0005	13.7424
	B	A	-5.0524*	1.83309	.019	-9.4233	-.6814
		C	4.3190	1.83309	.054	-.0519	8.6900
	C	A	-9.3714*	1.83309	.000	-13.7424	-5.0005
		B	-4.3190	1.83309	.054	-8.6900	.0519

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

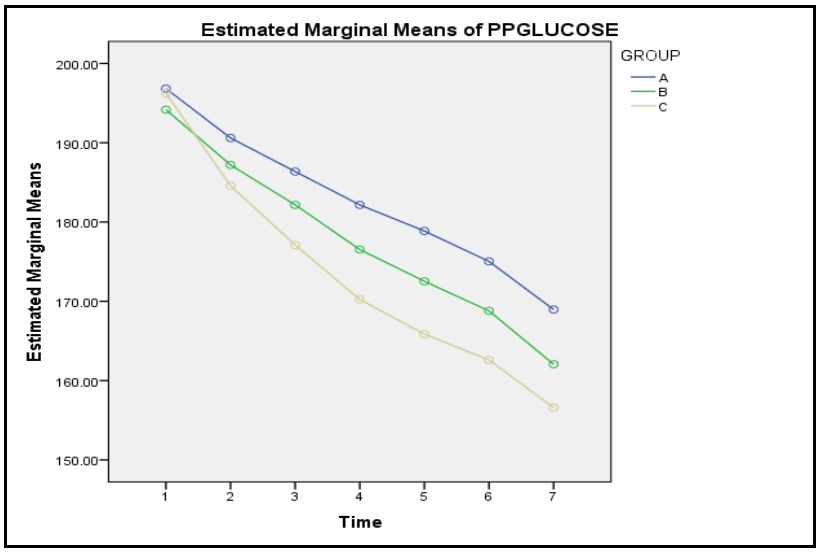

FIG.2: COMPARATIVE ANALYSIS OF GROUP A, B & C FOR POSTPRANDIAL BLOOD GLUCOSE LEVEL

HbA1c:

A mixed between- within subjects analysis of variance was conducted to compare the effects of three types of treatments (Group A, B & C) on HbA1c level across two time periods (zero day and ninety days). There was a significant interaction between time and type of treatments, Wilk's Lambda=0.598, F (2, 87) =29.294, p<0.001, partial eta squared=0.402 (**Table 9).**

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

Measure – HbA1c

Multivariate Tests [a]

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
Time	Pillai's Trace	.972	3046.394[b]	1.000	87.000	.000	.972
	Wilks' Lambda	.028	3046.394[b]	1.000	87.000	.000	.972
	Hotelling's Trace	35.016	3046.394[b]	1.000	87.000	.000	.972
	Roy's Largest Root	35.016	3046.394[b]	1.000	87.000	.000	.972
Time * Group	Pillai's Trace	.402	29.294[b]	2.000	87.000	.000	.402
	Wilks' Lambda	.598	29.294[b]	2.000	87.000	.000	.402
	Hotelling's Trace	.673	29.294[b]	2.000	87.000	.000	.402
	Roy's Largest Root	.673	29.294[b]	2.000	87.000	.000	.402

a. Design: Intercept + Group
Within Subjects Design: Time
b. Exact statistic

There was a significant main effect for time, Wilk's Lambda=0.028, F (1, 87) =3046.394, p<0.001, partial eta squared=0.972 (**Table 9**), with all groups showing a reduction in HbA1c level across the two time periods (**Table 10**).

TABLE 10:HBA1C (%) FOR ALL THE THREE GROUPS ACROSS TWO TIME PERIODS

	Group A (Only oral Hypoglycemic agent used)			Group B (Kasni crude seed powder & Oral Hypoglycemic agent used)			Group C (Decoction of Kasni seed powder & Oral Hypoglycemic agent used)		
Time Periods	M	SD	N	M	SD	N	M	SD	N
1. Zero day	7.5167	.29371	30	7.4633	.27852	30	7.5133	.24877	30
2. Ninety days	6.6567	.17750	30	6.4400	.14044	30	6.3033	.13767	30

The main effect comparing the three type of treatments was significant, F (2,87) =6.259, p=0.003 (p<0.05), partial eta squared=0.126, suggesting difference in the effectiveness of the three treatments (**Table 11**).

TABLE 11: ANALYSIS OF BETWEEN GROUP EFFECTS

Measure: HbA1c

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	8775.257	1	8775.257	105813.908	.000	.999
Group	1.038	2	.519	6.259	.003	.126
Error	7.215	87	.083			

Post hoc Tukey HSD test is showing that there is a significant difference between group A & B (p=0.032) and group A & C (p=0.003) (**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 HbA1c level of selected patients.

TABLE 12: MULTIPLE COMPARISONS GROUP A, B & C FOR HBA1C (%)

Measure: HbA1c

	(I) GROUP	(J) GROUP	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	A	B	.1350*	.05258	.032	.0096	.2604
		C	.1783*	.05258	.003	.0530	.3037
	B	A	-.1350*	.05258	.032	-.2604	-.0096
		C	.0433	.05258	.689	-.0820	.1687
	C	A	-.1783*	.05258	.003	-.3037	-.0530
		B	-.0433	.05258	.689	-.1687	.0820

Based on observed means.

The error term is Mean Square(Error) = .041.

* The mean difference is significant at the .05 level.

Profile plot is showing that Kasni seed powder decoction with oral hypoglycaemic agent is more effective than Kasni crude seed powder with oral hypoglycaemic agent in decreasing HbA1c level (**Fig. 3**).

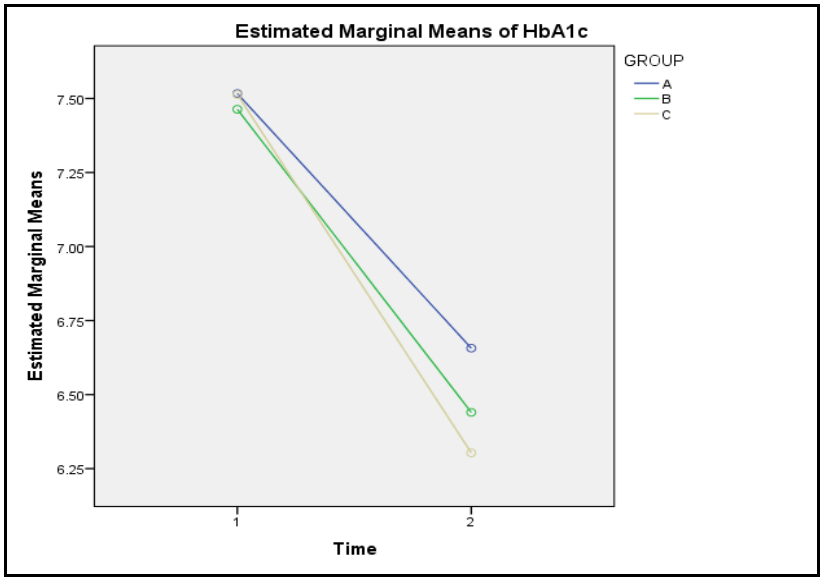

FIG. 3: COMPARATIVE ANALYSIS OF GROUP A, B & C FOR HBA1C (%)

DISCUSSION: Though number of studies have been conducted on Kasni (*Cichorium intybus*) for its therapeutic potential, however, present study is the first of its kind regarding the effects of Kasni seeds on fasting blood glucose (FBG), postprandial blood glucose (PPBG) and Glycosylated/glycated hemoglobin (HbA1c) of type 2 diabetes mellitus patients with poor glycemic control (HbA1c>7%).

Results obtained in the present study shown that reduction in FBG were more (P<0.05) in Kasni treated group B (19%) and C (21%) as compared to standard group A (16%); similarly reduction in PPBG were more (P<0.05) in Kasni treated group B (17%) and C (20%) as compared to standard group A (14%). HbA1c level was maximally reduced in group C (16%) followed by group B (14%) as compared to standard group A (11%). Significant improvement in HbA1c indicates that Kasni seeds can be used as add on therapy to those patients whose glycemic control cannot be achieved by conventional drugs.

Hypoglycemic drug Metformin (Glycomet SR), a biguanide agent, was used for this study. Glycomet SR (Metformin) was the standard hypoglycemic drug chosen for the present study because of added advantages like it lowers plasma glucose primarily 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 is the only therapeutic agent that has been demonstrated to reduce macrovascular events in type 2 diabetes mellitus[11].

Based on various animal models multiple mechanisms have been proposed so for regarding hypoglycemic activity of Kasni (*Cichorium intybus).* Caffeic acid and chlorogenic acid have been described by Tousch *et al*. as potential antidiabetic agents by increasing glucose uptake in muscle cells. These two compounds were also capable to stimulate insulin secretion from an insulin-secreting cell line and islets of langerhans. The other compound, chicoric acid, a potential antidiabetic agent, revealing both insulin-sensitizing and insulin-secreting properties [12]. Pushparaj et al. reported that administration of ethanol extract of *Cichorium intybus* whole plant, notably attenuated the serum glucose levels in the oral glucose tolerance test and hepatic glucose-6-phosphatase activity was found to be reduced in extract-treated diabetic rats as compared to untreated male Sprague-Dawley diabetic rats. The decrease in the hepatic glucose-6-phosphatase activity could decrease hepatic glucose production, which in turn consequences in lower concentration of plasma glucose in ethanolic extract of *Cichorium intybus*-treated diabetic rats[13].

Ghamarian et al. 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 prevented weight loss in both early-stage and late stage diabetes in rats. Diabetic animals treated with Chicory, resisted excessive increase in fasting plasma glucose (assessed by glucose tolerance test). In early-stage diabetic rats, chicory treatment led to the enhancement in insulin levels pointing toward the insulin-sensitizing action of chicory [14].

Asl *et al*. has also reported that *Cichorium intybus* L. increase glucose uptake and improve insulin sensitivity through inhibiting protein tyrosine phosphatase 1B (PTP1B) in adipogenic insulin signaling cascade both *in vitro* and *in vivo* [5]. Kaskoos RA reported that aqueous extract of Kasni (*C. intybus*) exhibited only moderate dose dependent hypoglycemic activity in STZ-induced diabetic rats. He ruled out the mechanism via intestinal delay or inhibition of glucose and any regeneration of pancreatic β cells but supported extra pancreatic mode of action and insulinotropic action of extract [8]. Hardeep *et al*. also found hypoglycemic action of methanolic extract of chicory roots in Streptozocin induced diabetic rats[15].

HbA1c is a glycated form of hemoglobin that is produced on hemoglobin's exposure to plasma glucose in a non-enzymatic glycation pathway. HbA1c also increases with the increase of plasma glucose. This is utilized as a marker for average plasma glucose levels over the previous months prior to the estimation. HbA1c denotes average plasma glucose over the prior 8 to 12 weeks [16]. It can be estimated at any time of the day and does not need any special condition such as fasting. These characteristics have made it the preferred test for evaluating glycaemic control in people with diabetes. Now-a-days, there has been significant importance in using it as a diagnostic test for diabetes mellitus and as a screening tool for individuals at high risk of diabetes[17]. In patients

with poorly controlled diabetes, the quantities of these Hb1Ac are much higher than in healthy people. Findings of present study denotes that Kasni seed preparations are effective in decreasing fasting, postprandial blood glucose and HbA1c levels of newly diagnosed type 2 diabetes mellitus patients. The study also revealed that partially purified preparations of Kasni seeds (Kasni seed powder decoction) is more effective than crude Kasni seed powder.

The use of Kasni seed preparations in primary prevention of hyperglycaemia in patients with type 2 diabetes mellitus could be more helpful after few more investigations such as herb-drug interactions *in vivo*, specific ingredient responsible and to determine the precise molecular mechanism of action of Kasni (*C. intybus*).

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