COMPARATIVE EVALUATION OF BGR-34 AND SITAGLIPTIN IN DIABETIC SUBJECTS-OPEN LABELLED RANDOMISED PARALLEL CLINICAL STUDY

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ABSTRACT

This article is mainly concerned with the simultaneous open model clinical study of the drug named sitagliptin, a potent hyperglycaemic drug against a novel entity of the natural origin BGR-34 in diabetic subjects. This was a 3-month randomized, parallel, comparative study. One hundred subjects were planned to be included in the study. The patients were randomly divided into two groups and according to the appropriate sample size analysis, both groups consisted of 100 patients, following the inclusion and exclusion criteria. A total of 90 patients (both male and female) of the mean patient age 30-65 years with the type 2 diabetes were enrolled in the phase 4 of this study and then the data were analyzed on the basis of the different test which included HbA1c (glycated haemoglobin), RBS (random blood sugar), FBS (fasting blood sugar) and PPG (postprandial glucose) values. After completion of the data calibration, the results were analyzed and as a result 10-20% decreased values of HBA1C values accompanied with the RBS, FBS and PPG values were seen in the patients undergoing a 12-week course with BGR-34. Based on the results obtained in the present study, it can be concluded that BGR-34 is effective in reducing high blood sugar levels and this reflects that the BGR-34 therapy is more effective drug in the treatment of diabetes suggesting that it is better in efficacy, and reliability with little or no adverse effects.

***Keywords*:** *diabetes mellitus, blood glucose regulator-34, DPP-4 inhibitors, hyperglycemia, sitagliptin.*

SAŽETAK

Ovaj rad se uglavnom bavi simultanom kliničkom studijom otvorenog tipa za lek Sitagliptin, koji je jedan jak hiperglikemijski lek nasuprot novog entiteta prirodnog porekla BGR-34 kod dijabetičara. Ovo je tromesečna randomizovana paralelna komparativna studija. Planirano je da 100 pacijenata bude uključeno u studiju. Pacijenti su nasumično podeljeni u dve grupe i prema odgovarajućoj analizi veličine uzorka, obe grupe su se sastojale od 100 pacijenata i pratile su kriterijume inkluzije i ekskluzije. Ukupno 90 pacijenata (muškaraca i žena), prosečno godište 30 – 65 godina sa dijabetesom tip 2 su bili uključeni u četvrtu fazu ove studije i onda su podaci analizirani na osnovu različitog testa koji je obuhvatio vrednosti HbA1c (glikolizirani haemoglobin), RBS (nasumični nivo šećera u krvi), FBS (nivo šećera u krvi pre jela) i PPG (postprandijalni nivo glukoze). Posle kompletiranja, kalibrisanih podataka, rezultati su analizirani i kao rezultat 10-20% smanjene vrednosti HBA1C praćene sa RBS, FBS i PPG vrednostima su primećene kod pacijenata koji su bili podvrgnuti BGR-34 u toku 12 nedelja. Zasnovane na rezultatima dobijenim u sadašnjoj studiji, može se zaključiti da je BGR-34 efikasan u smanjenju visokih nivoa šećera u krvi i ovo pokazuje da je terapija sa BGR-34 efikasniji lek u lečenju dijabetesa što sugeriše da je bolji što se tiče delovanja i pouzdanosti sa malo ili bez neželjenih dejstava.

***Ključne reči*:** *dijabetes melitus, regulator-34 glukoze u krvi, DPP-4 inhibitori, hiperglikemija, sitagliptin.*

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INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is not a new entity, which requires any introduction, as it has been affecting individuals globally for decades. The presentation of the aforementioned metabolic condition involves hyperglycemia and glucose intolerance which result from the lack of insulin secretion, defective insulin action or perhaps both (1). Such complications arise due to the derangements in the regulatory systems for storage and mobilization of the metabolic fuel, including the catabolism and anabolism of carbohydrates, lipids and proteins emanating from the defective insulin secretion, insulin action, or both. In addition to this, the intake of high calories and physical inactivity potentially increase the likelihood of T2DM (2). It has been found that around 366 million people had T2DM in 2011 (3) and it is expected to reach the number of 552 million by the year 2030. The incidence of T2DM results most commonly due to the environmental as well as lifestyle factors and varies geographically (4). Individuals aged between 45 years to 64 years are at a higher risk to be affected with this metabolic condition (5). T2DM can further trigger chances of developing macro- and micro-vascular complications associated with the elevated blood sugar such as cardiovascular diseases, peripheral vascular diseases, stroke, neuropathy, renal failure, retinopathy etc (6). Furthermore, various genetic, environmental and behavioural factors are responsible for the increased prevalence of diabetes mellitus (5). Urbanization, aging, physical inactivity, obesity, etc are exponentially resulting in the increased prevalence of diabetes mellitus worldwide. Numerous oral hypoglycaemic agents (OHA's) have been available at the market since quite a long time for the effective management of T2DM. One of the therapeutic modalities named "Sitagliptin", which belongs to the class of Dipeptidyl Peptidase-4 (DPP-4) inhibitor, has been found to be relatively effective in the management of T2DM with a low risk of hypoglycaemia. It brings about inhibition of DPP-4 enzyme. DPP-4 is a complex molecule that is expressed in various cell types. It selectively degrades the levels of two incretins i.e. Glucose-dependent insulinotropic polypeptide (GIP) and glucose-like peptide-1 (GLP-1) in the body that is released into the circulation after meals and potentiates the secretion of glucose dependent insulin from pancreatic β cells. GLP-1 also inhibits the secretion of glucagon and gastric emptying. The activation of incretin receptor stimulates the secretion of insulin in the presence of elevated blood glucose. Sitagliptin lowers the activity of DPP-4 and increases the levels of intact GIP and GLP-1 following meals. Moreover, it reduces the blood glucose levels without causing significant hypoglycaemia (7). However, recently, there has been a trend of opting for traditional medicines instead of allopathic medication for the management of various chronic diseases and T2DM is not an exception. There are several works in the literature that are reviewed by many authors of herbal drugs for the treatment of diabetes [8]. Recently, The Council of Scientific & Industrial Research (CSIR) has developed a herbal drug "BGR-34", a Blood Glucose Regulator which comprises 34 vital plants. It maintains blood glucose, relieves symptoms, decreases the occurrence of diabetic complications and is highly safe and reliable.

The current study assessed the safety and efficacy of BGR-34 (620mg) in patients with the type 2 diabetes mellitus against Sitagliptin (100mg) with the inadequate glycaemic control on diet and exercise.

SUBJECTS AND METHODS

Study designs & Intervention

The current study was a randomized, parallelgroup, comparative study conducted over a period of 12 weeks in order to determine the efficacy and safety of the new molecular entity, BGR-34 at a tertiary care teaching hospital of North India. The Indian population was selected for the study in which the subjects were divided into two groups – Group 1 and Group 2 where the patients were receiving 100 mg of Sitagliptin once a day and 620 mg of BGR-34 once a day respectively for the duration of 12 weeks. In addition to this, the patients received counseling on a diet consistent with the American Diabetes Association recommendations for the study entry. There were a total of three followup visits along with the screening and baseline visit. The study subjects were assessed for any kind of side effects and safety during each and every visit. The screening data were reviewed to determine the subject eligibility. It was the responsibility of the principal investigator to educate or inform the subjects about the study and its outcomes. The study protocol was approved under the Gian Sagar Medical College and Hospital's Ethics Committee and was in compliance with the Declaration of Helsinki. A written informed consent was obtained from the patients who met all inclusion criteria and none of the exclusion criteria. After the statistical analysis and interpretation of the data, all the records were registered and reported appropriately to the associated higher authorities.

Study endpoints

The primary endpoint was to assess the efficacy of BGR 34 by achieving the diabetic control. This was assessed by a reduction in the levels of glycosylated haemoglobin (HbA1c) in the study subjects; the key secondary endpoints included the assessment of Fasting Blood Sugar (FBS), Random Blood Sugar (RBS) and Post-Prandial Blood Sugar (PPBS). The safety assessment data for adverse drug reactions (ADRs), physical examinations, vital signs and body weight were maintained throughout the study. The causality assessment of ADRs was based on the World Health Organization (WHO) – Uppsala Monitoring Centre (UMC) Causality assessment scale. The baseline laboratory tests were performed before initiation of the study period such as alanine aminotransferase, aspartate aminotransferase, total bilirubin, alkaline phosphatase, creatinine, haematology and urinalysis.

Study population

For the enrolment of the subjects in this double blind study, screening was performed. The enrolled subjects should be – the Indian population aged 30-65 years; diagnosed with T2DM; Fasting Blood Sugar (FBS) ranges from 126 mg/dl – 200 mg/dl; Post-Prandial Blood Sugar (PPBS) ranges from >200 mg/dl – 350 mg/dl; HbA1c ranges from 6.5 - >8.5 and not receiving any corticosteroids; Body Mass Index (BMI) > 25Kg/M^2 , the absence of any chronic disease; ready to give audio visual consent for the study participation. The individuals receiving insulin for the management of T2DM; suffering from the acute/chronic/ debilitating comorbid conditions; pregnant & lactating females; participation in any other clinical trial within the last 30 days; subjects with an allergy to investigation product; the individual meeting the inclusion criteria but unwilling to participate, were excluded from the study. The patients were randomly divided into two groups (Group 1 & Group 2) and according to the appropriate sample size analysis, both groups consisted of 100 patients, following the Inclusion and Exclusion criteria.

Procedure

A total of 100 outpatients were enrolled from Gian Sagar Medical College and Hospital, Banur. The primary clinical measurements were the glycosylated hemoglobin (HbA1c) levels, Random Blood Sugar (RBS) levels, Fasting Blood Sugar (FBS) levels and Postprandial Glucose (PPG) levels tested within 3 months at the time of the enrollment and after each visit i.e. after the 4th week, 8th week and 12th week. Physicians collected the patients' demographic data and clinical characteristics at the baseline for all potentially eligible individuals. The study parameters were assessed using laboratory results.

Statistical analyses

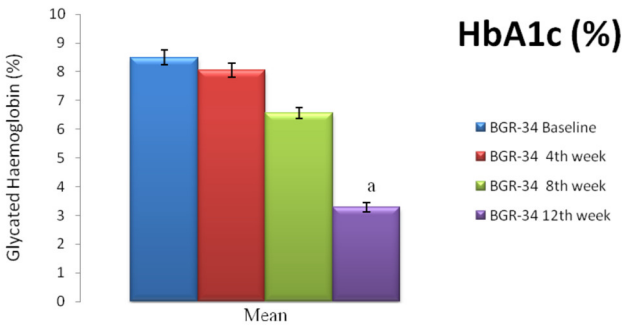
Continuous values were analyzed and represented as the mean, standard deviation (SD) and standard error mean (SEM). The demographic data and background information were recorded following the multivariate logistic regression analysis. SPSS (version 14.0) statistical software was used only for analyses. In this, the analysis was performed using the paired t tests, with a significance level of $p < 0.05$.

RESULTS

Glycosylated haemoglobin (HbA1c)

As depicted in Figure 1(A), the subjects receiving BGR-34 for the management of T2DM had a significant glycemic control over the period of 12 weeks. BGR -34 was able to reduce the mean HbA1c values significantly from the mean baseline HbA1c values (8.499% ± 0.25%) over the period of 4 weeks (8.061% ± 0.24%), 8 weeks (6.56% ± 0.196%) and 12 weeks (6.27% ± 0.111%).

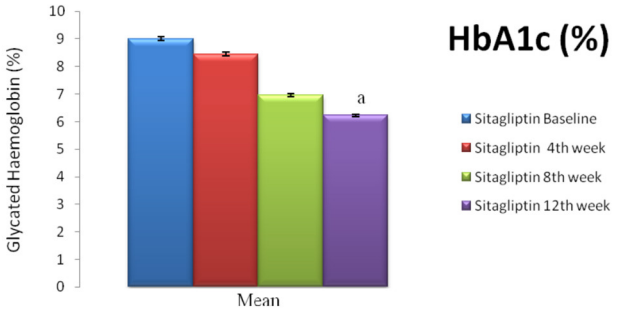
Figure 1 (A). Effect of BGR-34 on HbA1c over the period of 4, 8 and 12 weeks



a ($p<0.01$) vs. HbA1c % at the 12th week BGR-34

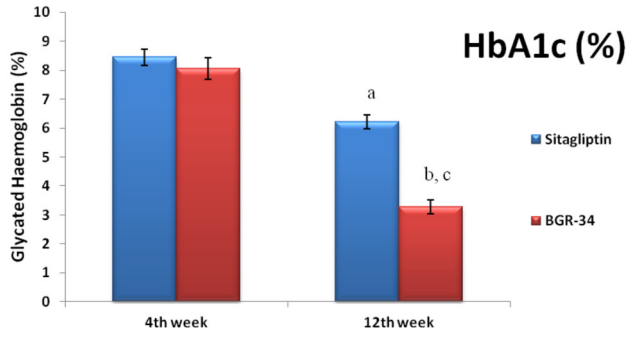
Similarily, sitagliptin also produced a similar effect by reducing the mean HbA1c values when compared to the mean baseline values of HbA1c (9.001% ± 0.073%) to 8.44% ± 0.074% (Over 4 weeks), 6.97% ± 0.057% (Over 8 weeks) and 6.22% ± 0.038% (Over 12 weeks) as represented in Figure 1 (B). A reduction in the levels of HbA1c in the BGR-34 group compared to their respective baseline value was significant with a p value of (<0.001). As represented in Figure 1(C), in the statistical comparison of glycemic control with BGR-34 and Sitagliptin over a period of 12 weeks, it was observed that the glycemic control with BGR-34 was more significant than Sitagliptin (P<0.001).

Figure 1(B). Effect of Sitagliptin on HbA1c over the period of 4, 8 and 12 weeks



a ($p<0.01$) vs. HbA1c % at the 12th week Sitagliptin

Figure 1(C). Effect of BGR-34 and Sitagliptin after 4 and 12 weeks on HbA1c (HbA1c) values in type 2 diabetic patients.

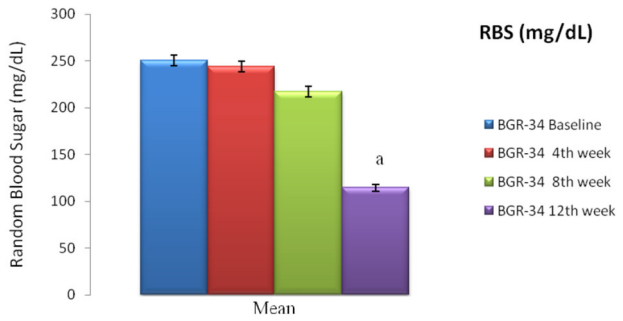


a ($p<0.05$) Vs HbA1c at the 4th week Vs 12th week (Sitagliptin)
b ($p<0.05$) Vs HbA1c at the 12th week (BGR-34)
c ($p<0.001$) Vs HbA1c at the 12th week (Sitagliptin Vs BGR-34)

Random Blood Sugar (RBS)

As depicted in Figure 2(A), the BGR-34 treatment for the period of 12 weeks produced a significant difference from the baseline RBS (250.32 mg/dl ± 5.645 mg/dl). The observed values of RBS reduced significantly in the study population over the period of 4 weeks, 8 weeks and 12 weeks which was 243.76 mg/dl ± 5.605 mg/dl, 217.24 mg/dl ± 5.426 mg/dl, and 114.4 mg/dl ± 2.596 mg/dl respectively. The study population receiving Sitagliptin also produced a similar effect as BGR-34, as the RBS value declined over the period of 12 weeks.

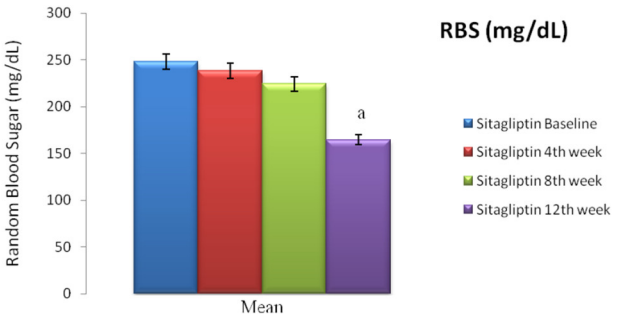
Figure 2 (A). Effect of BGR-34 on RBS over the period of 4, 8 and 12 weeks



a ($p<0.001$) Vs RBS at the 12th week BGR-34

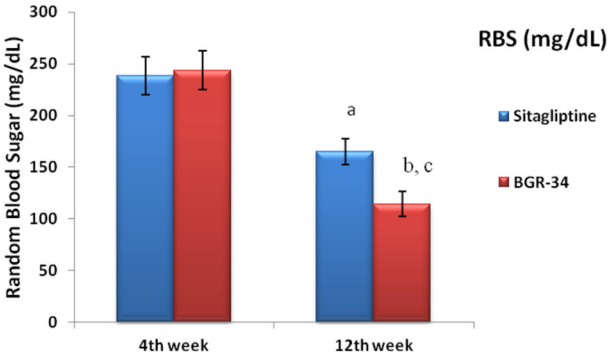
The values of RBS over the period of 4 weeks, 8 weeks and 12 weeks when compared to the baseline RBS (248.2 mg/dl ± 8.174 mg/dl) were observed as 238.46 mg/dl ± 7.947 mg/dl, 224.46 mg/dl ± 7.724 mg/dl, 164.66 mg/dl ± 5.327 mg/dl as depicted in Figure 2(B). As shown in Figure 2(C), in the comparative reduction of RBS in both study groups, it was observed that the group receiving BGR-34 had a statistically significant reduction in RBS when compared to the group receiving Sitagliptin ($P<0.001$) over the period of 12 weeks.

Figure 2(B). Effect of Sitagliptin on RBS over the period of 4, 8 and 12 weeks



a ($p<0.01$) Vs RBS at the 12th week Sitagliptin

Figure 2(C). Effect of BGR-34 and Sitagliptin after 4 and 12 weeks on Random Blood Sugar (RBS) values in type 2 diabetic patients.



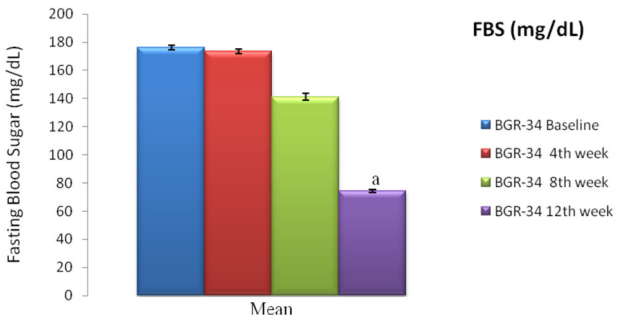
a ($p<0.05$) Vs RBS at the 4th week Vs 12th week (Sitagliptin)
b ($p<0.001$) Vs RBS at the 4th Vs 12th week (BGR-34)
c ($p<0.005$) Vs RBS at the 12th week (Sitagliptin Vs BGR-34)

Fasting Blood Sugar

The BGR-34 treatment for the period of 12 weeks produced a significant difference from the baseline FBS (176.4 mg/dl ± 1.685 mg/dl) as depicted in Figure 3(A). The observed values of FBS reduced significantly in the study population over the period of 4 weeks, 8 weeks and 12 weeks which were 173.3 mg/dl ± 1.607 mg/dl, 141.22 mg/dl ± 2.672 mg/dl, and 74.28 mg/dl ± 0.889 mg/dl respectively. The study population receiving Sitagliptin also produced a similar effect as BGR-34, as the FBS value declined over the period of 12 weeks. The values of FBS over the period of 4 weeks, 8 weeks and 12 weeks when compared to the baseline FBS (177.12 mg/dl ± 4.729 mg/dl) were observed as 165.4 mg/dl ± 4.367 mg/dl, 151.1 mg/dl ± 4.226 mg/dl, 151.1 mg/dl ± 4.226 mg/dl as depicted in Figure 3(B). As shown in Figure 3(C), in the comparative reduction of FBS in both study

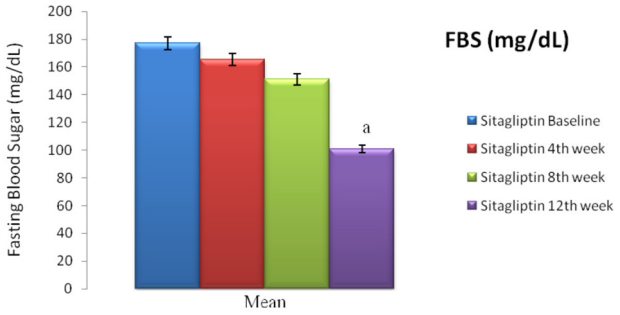
groups, it was observed that the group receiving BGR-34 had a statistically significant reduction in FBS when compared to the group receiving Sitagliptin (P<0.001) over the period of 12 weeks.

Figure 3(A). Effect of BGR-34 on FBS over the period of 4, 8 and 12 weeks



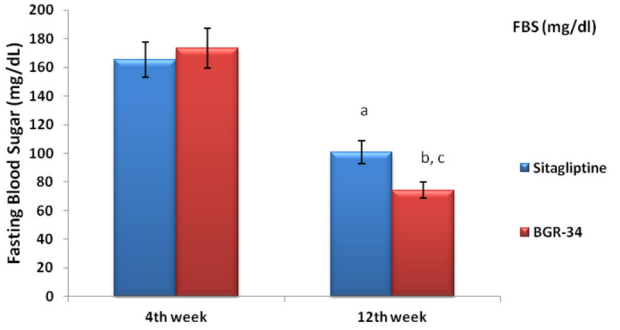
a (p<0.001) Vs FBS at the 12th week BGR-34

Figure 3(B). Effect of Sitagliptin on RBS over the period of 4, 8 and 12 weeks



a (p<0.005) Vs FBS at the 12th week Sitagliptin

Figure 3(C). Effect of BGR-34 and Sitagliptin after 4 and 12 weeks on Fasting Blood Sugar (FBS) values in type 2 diabetic patients.

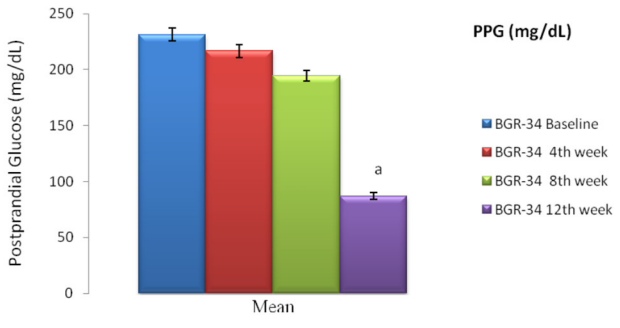


a (p<0.05) Vs FBS at the 4th week Vs the 12th week (Sitagliptin)
b (p<0.001) Vs FBS at the 12th week (BGR-34)
c (p<0.005) Vs FBS at the 12th week (Sitagliptin Vs BGR-34)

Postprandial Glucose

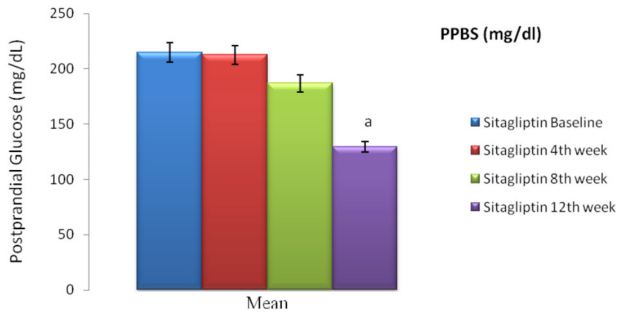
A significant change was observed in Post Prandial Blood Sugar (PPBS) in the patients receiving the BGR-34 treatment for the period of 4 weeks (216.84 mg/dl ± 5.773 mg/dl), 8 weeks (186.94 mg/dl ± 7.667 mg/dl) and 12 weeks (87 mg/dl ± 2.273 mg/dl) when compared to the baseline PPBS (231.38±5.78). A similar pattern was observed with Sitagliptin, as it was observed that PPBS declined significantly from 214.92 mg/dl ± 8.544 mg/dl to 212.58 mg/dl ± 8.478 mg/dl in 4 weeksand 8 weeks respectively and 129.54 mg/dl ± 4.725 mg/dl in the 12thweek(Figure 4 A, B). As shown in Figure 4(C), in the comparative reduction of PPBS in both study groups, it was observed that the group receiving BGR-34 had a statistically significant reduction in FBS when compared to the group receiving Sitagliptin (P<0.001) over the period of 12 weeks. The adverse effects were observed in 4% (2/50) of patients in the BGR-34 treated group and in 14% (7/50) of the patients in the Sitagliptin treated group. The patients receiving BGR-34 reported the gastric problem in 4% (2/50) whereas in the Sitagliptin treated group, the patients experienced the abdominal pain in 5% (*n* =1), nasophayngitis in 4% (*n* =2), GIT upset and constipation in 4% (*n*=2) nausea and diarrhoea were observed in two patients (4%). In the present study, to assess the safety of BGR-34 and Sitagliptin, the analyses of various biochemical parameters were done which revealed no significant changes in the patients. The treatment with Sitagliptin had a neutral effect on the body weight. However, in the Sitagliptin treated group, a slight increase was observed in the white blood cell count, primarily due to a small increase in the absolute neutrophil count and in the uric acid levels, but which were not significant. In addition to this, all other safety parameters viz. serum creatinine, the total leukocyte count, the differential leukocyte count, SGOT and SGPT, haemoglobin did not show any significant change. The present study confirms that the drugs were well tolerated and the patients showed full compliance toward the treatment during the study.

Figure 4(A). Effect of BGR-34 on PPBS over the period of 4, 8 and 12 weeks



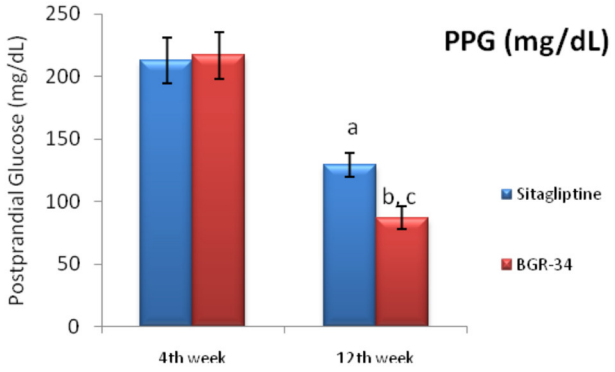
a (p<0.001) Vs PPG at the 12th week BGR-34

Figure 4(B). Effect of Sitagliptin on PPBS over the period of 4, 8 and 12 weeks



a ($p<0.001$) Vs PPG at the 12th week Sitagliptin

Figure 4(C). Effect of BGR-34 and Sitagliptin after 4 and 12 weeks on Post Prandial Blood Sugar (PPBS) values in type 2 diabetic patients.



a ($p<0.05$) Vs PPG at the 4th week Vs 12th week (Sitagliptin)
b ($p<0.001$) Vs PPG at the 12th week (BGR-34)
c ($p<0.05$) Vs PPG at the 12th week (Sitagliptin Vs BGR-34)

DISCUSSION

Diabetes mellitus is a highly prevalent metabolic disorder that has affected nearly half of the population around the world. It is characterised with significantly high glucose levels in the blood which is associated with its typical clinical presentation of polyuria, polydipsia and polyphagia. Diabetes mellitus when left untreated may increase the likelihood of various metabolicchanges resulting invarious micro- and macro-vascular complications affectingthe eyes, kidney, heart and nerves (9). With availability of numerous oral therapeutic agents at the market, managing T2DM is still challenging and requires strict discipline in the diet and lifestyle. Numerous studies have been conducted implicating various therapeutic agents, currently available for the management of T2DM to assess their safety and efficacy. The available therapeutic modalities act either by increasing the secretion of insulin from pancreas or increasing the glucose uptake and decreasing gluconeogenesis, resulting in the reduced plasma glucose concentration (10). A regular and optimum control of the glucose levels can decrease the progression of the disease and further reduce the chances of occurrence of complications. The available oral hypoglycaemic drugs do not restore normal glucose homeostasis for a longer period and they are not free from side effects such as hypoglycemia, kidney diseases, GIT problems, hepatotoxicity, heart risk problems, insulinoma and they have to be taken for the rest of life (11). However, the treatment with herbal medications is trending nowadays. Various herbal drugs have also shown beneficial effects in controlling the blood glucose levels in the patients suffering from T2DM (10). Unfortunately, the role of herbal agents in the management of T2DM is still questionable due to the lack of clinical data on their safety and efficacy. Thus, the present study was conducted in order to generate the evidence regarding efficacy and safety of the herbal drug, "BGR-34" with the established oral hypoglycaemic agent "Sitagliptin" in the patients with the type 2 diabetes mellitus. Sitagliptin phosphate has already been the US FDA approved modality for the management of T2DM since 2006 (7). Sitagliptin, with already proven safety and efficacy profile in managing T2DM through several clinical studies, has an established market worldwide. Many double-blind studies were conducted in which Sitagliptin was compared to another DPP-4 inhibitor as a monotherapy or as an add-on therapy; with other oral hypoglycaemic drugs (12). Several doses of Sitagliptin were used to check the efficacy of the drug at various doses in trials lasting for 18-52 weeks (13). Sitagliptin given at doses of 100 mg and 200 mg was found to be significant (14) in reducing mild to moderate hyperglycemia; improving glycosylated haemoglobin; fasting plasma glucose; and the post prandial glucose levels. A similar study was conducted for 24 weeks, in which Sitagliptin significantly reduced HbA1c, fasting blood glucose, and post-prandial glucose ($p < 0.001$). In the same study, 100 mg and 200 mg of Sitagliptin were compared to the subjects receiving placebo, where 41% and 45% of the study population received Sitagliptin 100 mg and 200 mg respectively and only 17% of the study population received placebo. The result depicted a significant correlation between HbA1c (baseline) and the treatment with higher efficacy in the patients with higher baseline HbA1c (15). Furthermore, in the study, 100 mg dose of Sitagliptin was found to be well tolerated in the type 2 diabetic patients and provided an effective and sustained control of HbA1c, fasting glucose and post-prandial glucose. It was also found that Sitagliptin carries a lower risk of hypoglycaemia (16). Moreover, it has also been found that 100 mg dose of Sitagliptin once daily significantly lowers the glycemic level and β-cell functions of pancreas in the patients who had an inadequate control of the glycemic levels with Glimepiride or Glimepiride plus Metformin therapy. It is clear from most of the trails that sitagliptin produces the adequate improvements in the glycemic parameters. Apart from this, sitagliptin when given as a monotherapy lowers HbA1c levels up to 0.94%. However, when used in the combination with other oral hypoglycaemic drugs, it can provide an additional reduction in the glycemic levels in the body (17).

On the other hand, the preclinical study on BGR-34 has proven it to be safe and effective, with clinical studies

demonstrating 67% of success (NBRI). A doubleblind study for BGR-34 was conducted by the CSIR to check its efficacy in the patients with the type 2 diabetes mellitus at Aggarwal Hospital, New Delhi. There were, a total of 48 patients selected for the study consisting of 30 males and 18 females after applying the inclusion as well as exclusion criteria. It was conducted for a period of 16 weeks. The patients were divided into two groups in which 24 patients were on the BGR-34 therapy and other 24 patients were in the placebo group. The biochemical results revealed that highly significant results were obtained in 15 patients receiving BGR-34. There were relatively lower levels of blood sugar. However, there was no reduction in glycosylated haemoglobin in the patients receiving placebo. Instead, a significant increase was observed in the subjects receiving BGR-34 during a 16week study. The present study was a randomized, parallel, comparative study in which the subjects were randomly selected. The outcome of the study revealed that there was a significant reduction in HbA1c, Random Blood Sugar (RBS), Fasting Blood Sugar (FBS) and Postprandial Glucose (PPG) with BGR-34 when compared to Sitagliptin. BGR-34 acts through several mechanisms and maintains the optimum blood glucose levels, relieves the symptoms associated with T2DM and reduces the chances of complications and imparts a good quality of life in the patients with high blood sugar levels. The possible reason for better efficacy could be due to its several nutritive phytoconstituents and antioxidants which protect β-cells from damage, promote the repair and regeneration of β-cells. Thus, the insulin production is increased by improving the functional capacity of β-cells.

CONCLUSION

Based on the results obtained in the present study, it can be concluded that BGR-34 is effective in reducing high blood sugar levels and is more potent and efficacious in decreasing the glycemic levels possibly by modulating the insulin release and strengthening the β-cell functional capacity. It also exerts a powerful anti-oxidant action which prevents the development of diabetic complications. This reflects that the BGR-34 therapy is more effective drug in the treatment of diabetes suggesting that it is better in efficacy, reliability and affordability with little or no adverse effects. From the present study, it has emerged that this treatment favourably contributes to the health effective benefits by inhibiting the disease progression and fulfilling the alternate goals of the management of diabetes mellitus. Strict glycaemic control favours the goals of managing diabetes mellitus.

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CONFLICT OF INTERESTS

There are no conflicts of interest.

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LITERATURE

1. Singh R, Rao HK, Singh TG. Advanced glycated end products (ages) in diabetes and its complications: an insight. Plant Arch. 2020; 20(1): 3838-3841.
2. Sharma VK, Singh TG. Chronic Stress and Diabetes Mellitus: Interwoven Pathologies. Curr Diabetes Rev. 2019;16(6): 546-556.
3. Olokoba AB, Obateru OA, Olokoba LB. Type 2 Diabetes Mellitus: A Review of Current Trends. Oman Med J. 2012; 27(4): 269–273.
4. Chen L, Magliano DJ, Zimmet PZ. The worldwide epidemiology of type 2 diabetes mellitus – present and future perspective. Nat. Rev. Endocrinol. 2011; 8(4):228-36.
5. Singh R, Rao HK, Singh TG. Neuropathic pain in Diabetes Mellitus: Challenges and Future Trends. Obes Med. 2020; 18.100215.
6. Jothivel N, Ponnusamy SP, Appachi M. Antidiabetic activities of methanol leaf extract of Costus pictus D. Don in alloxan-induced diabetic rats. J health sci. 2007; 53(6):655-663.
7. Drucker D, Easley C, Kirkpatrick P. News and analysis. Nat Rev Drug Discov. 2007; 6:109-110.
8. Singh TG, Sharma R, Kaur A, Dhiman S, Singh R. Evaluation of renoprotective potential of Ficus religiosa in attenuation of diabetic nephropathy in rats. Obes Med. 2020; 19: 100268.
9. Al-masri IM, Mohammad MK, Tahaa MO. Inhibition of dipeptidyl peptidase IV (DPP IV) is one of the mechanisms explaining the hypoglycemic effect of berberine. J enzyme inhib med chem. 2009; 24(5):1061–1066.
10. Chinmay D, Deshmukh, Jain A. Diabetes Mellitus: A Review. Int. J. Pure App. Biosci. 2015; 3(3): 224-230.
11. Nathan DM, Buse JB, Davidson MB. Medical management of hyperglycemia in type 2 diabetes: a consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care. 2009; 32:193–203.
12. Pratley RE, Gilbert M. Targeting Incretins in Type 2 Diabetes: Role of GLP-1 Receptor agonists and DPP-4 inhibitiors. Rev of Diabet Stud. 2008; 5:73-94.
13. Amori RE, Lau J, Pittas AG. Efficacy and Safety of incretin therapy in type 2 diabetes: Systemic Review and Analysis. JAMA. 2007; 298:194-206.
14. Raz I, Hanefeld M, Xu L, Caria C, Williams-Herman DE, Khatami H. Efficacy and safety of the Dipeptidyl Peptidase-4 inhibitor Sitagliptin as monotherapy in patients with type 2 diabetes mellitus. Diabetologia. 2006; 49:2564-71.

15. Aschner P, Kipnes MS, Lunceford JK, Sanchez M, Mickel C, Williams-Herman DE. Effect of the Dipeptidyl Peptidase-4, inhibitor Sitagliptin as monotherapy on glycemic control in patients with type 2 diabetes. Diabetes Care. 2006; 29:2632-37.
16. Cherbonnel B, Karasik A, Liu J, Wu M, Menininger G. Efficacy and safety of the Dipeptidyl Peptidase-4 inhibitor Sitagliptin added to ongoing metformin therapy in patients with type 2 diabetes inadequately controlled with metformin alone. Diabetes Care. 2006; 29:2638-43.
17. Hermansen K, Kipnes M, Luo E, Fanurik D, Khataami H, Stein P. Efficacy and Safety of the dipeptidyl peptidase-4 inhibitor, Sitagliptin, in patients with type 2 diabetes inadequately controlled on glimepiride alone or on glimepiride and Metformin. Diabetes Obese Metab. 2007; 9:733-45.
18. Sharma VK, Singh TG, Insulin resistance and bioenergetic manifestations: Targets and approaches in Alzheimer's disease. Life Sci. 2020; 118401.