Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 6, 2021, Pages. 13304 – 13312
Received 25 April 2021; Accepted 08 May 2021.

A Preliminary Study on Antidiabtic Activity of Vincristine in Wistar Rat

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Abstract

The current exploration work was to explore the hyperglycemia movement of vincristine (1.5Milligram/ kilogram or 3 Milligram/ kilogram i.p).The anti-diabetic movement was assessed against Streptozotocin instigated diabetes in rodents. In case of streptozotocin instigated diabetes (3 mg/kg, i.p) is more effective comparison to 1.5 Milligram/ kilogram. But in case of hyperlipidemia in both low and high dose is more effective of vincristine (1.5 mg/kg or 3 Milligram/ kilogram i.p) diminish the level of cholesterol triglyceride low density containing lipid protein and high density containing lipid protein respectively. The exploration result shows that vincristine (1.5Milligram/ kilogram or 3 Milligram/ kilogram i.p).is having a huge enemy of against hyperglycemia, dyslipidemia.

Keywords- Vincristine, Hyperglycemia, Dyslipidemia, Streptozotocin, Diabetes.

INTRODUCTION

Diabetes mellitus is one of the major chronic non-infectious diseases in the world with a continuous enhance number of patients leads to a much more rigorous burden on the human population(1). It is also reported that DM becomes the third human cause of death next to cancer and cardiovascular disease. Multiple abnormal metabolic conditions like hyperglycemia, hyperlipidemia, hypertension, and obesity results in consequent cardiovascular diseases and diabetes mellitus (2).World Health Organization [WHO] has been reported that in 2019, there were 422 million peoples in the world suffering from the DM. DM became an important public health problem because its complications (3). Global diabetes prevalence in 2019 is estimated to be 9.3% (463 million people), rising to 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045. To provide global estimates of diabetes prevalence for 2019 and projections for 2030 and 2045.For the treatment of diabetes various category of allopathic and herbal drugs are available The current allopathic drugs used for treatment of diabetes possess the various adverse effects such as hypoglycemia, dizziness, headache, diarrhea, nausea, vomiting, flatulence, hyponatremia,

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pernicious anemia, lactic acidosis, liver toxicity, weight gain etc., Therefore, medicinal plants provide an attractive alternative for newer and more potent anti-diabetic agents avoid the side effects (4).

The anticancer drugs are a class of chemicals that are produced from the Madagascar periwinkle plant and have long been used in people with diabetes to treat hypoglycemia.Certainvinca alkaloids were discovered to cause stem cells inhibition in mice and life extension in rats with acute lymphoblastic leukaemia in the late 1950s. As a result, anti-mitotic marketers have become increasingly common in multi-agent chemotherapy protocols for a wide range of cancers, including all types of, lymphomas, sarcomas, neuroblastoma, and tumours of the kidney, liver, lung, mind, and breast, among others.(5)
On the other side, vinorelbine has an eight-member catharnine ring, as opposed to the nine-member earrings of the other vinca alkaloids, that allows for more potential to connect to mitotic spindles over axonal microtubules, resulting in less neuroinflammation dosage intensification .Vinorelbine is most frequently used to diagnose breast and non-small cell lung malignancies, and its dose-restricting effect is myelosuppression. Finally, vincristine was already encased in sphingomyelin and low-density lipoprotein cholesterol nanoparticles as a vincristine sulphate liposome injection (VSLI), which is marketed under the trade name Marqibo.This new vincristine approach was intended to allow for improved pharmacokinetics, better drug delivery to malignant cells, and dose intensificationIn 2012, the FDA approved it for the prevention of people with relapsed or refractory Philadelphia-chromosome's nasty primary lymphoblastic'sneoplasm.Vincristine does have a low bio—availability and is compounded as vincristine sulphate for intravenous administration. (6)

MATERIALS AND METHODS

Experimental rodents

Wistar rodents of either sex weighing between 150-200g were used for this examination. They were obtained in the AIBPS creature house Kanpur perceived by the Institutional Animal Ethics Committee (IAEC). Polypropylene limits were utilized to house (3 for each pen) the creature at body level of warmth of 28 ±50C and 12 hours light/dull cycle. Hindustan Lever chow pellets were used to take care of the creature and water not essential. The creatures were continued fasting medium – term going before the assessment and this examination was affirmed by IAEC for creature considers (1122/PO/Re/S/2007/CPCSEA) incorporate all structure utilized in the exploration.

Chemicals and drugs

Vincristine Injection, Batch No.- 2568003 was gotten from Axiommax oncology private Limited and Glibenclamide Tablet (Emcure Pharmaceutical Limited Batch No.SM ONAU024);Streptozotocine concentrates powder was purchased from Sigma Aldrich .

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Study design

Streptozotocin –induced diabetes in rats

Principle (Induction of Hyperglycemia)

After an overnight fast, wistar rodents were given a single intraperitoneal injection of 50 m/iligram/kilogramofStreptozotocin reconstituted in normal saline (0.9 percent).Blood glucose levels were evaluated in blood samples taken from tail vein puncture after 72 hours of Streptozotocin - induced diabetic administration using one touch Glucometer strips and an glucometer.Diabetic rats were chosen for the investigation if their fasting blood glucose level was greater than 300 miligram/decilitre.Groups were randomly assigned to one of seven groups after fasting for 12 hours (8 rodents in each group).The first group was used as a normal control (non-diabetic) and was given normal saline, whereas the second group was used as a diabetic control and was given a 5% Tween-80 suspension.Glibenclamide (500 micrograms per kilogramme, p.o.) was given to the third group.The fourth and fifth groups were given Vincristine at doses of 1.5 and 3 mg/kg, respectively (i.p)The vincristine treatment was continued once every day at 9:00 a.m. for a total of 24 days.On the 0th, 4th, 7th, 10th, and 24th days of treatment, body weight and blood sugar levels were measured.On the fifteenth day.All mice were anaesthetized with pentobarbital sodium (35 miligram /kilogram) and died by cervical decapitation, as outlined in Schedule 1 of the Animal Scientific Procedure Act 1986, with blood samples were drawn through heart fracture for physiological parameter examinations.Donated blood was centrifuged at 1500 rpm for 10 min to separate serum.On a UV-Spectrophotometer, total cholesterol, low density lipoproteins, high density lipoprotein triglycerides, and serum were tested using a Human kit from Germany(7,8).

Statistical analysis

All the utility of serum sugars, frame weight, and biological frameworks s had beendepictioned as mean ± S.E.M. For contrast of businesses, Student’s t-take a look atturned into used and whileextra than businesseshad been compared, one manner ANOVA accompaniedthroughDunnett’sposthocmore than onecontrasttake a look atturned into used. Differences amongbusinesseshad beentaken into considerationsizeable at $p<0.05$.

RESULTS AND DISCUSSION

Antihyperglycemic effect of *vincristine*

Alteration s in serum sugar degree in normal, diabetic and on remedy of diabetic rodents with numerous fractions of vincristine and glibenclamide are provided in desk 1. intraperitoneal injection administration vincristine (1.5and 30 miligram/kilogram) precipitated a giant ($p<0.01$, $n=6$; one manner ANOVA with

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Dunnett'sposthoc test) discount in serum sugar degreeas compared to diabetic control. intraperitoneal injection administration vincristine (1.5and 30 miligram/kilogram) reduced blood glucose degree from 477.7±18 to 244.3±22 miligram/deciliter and from 476.7±fifty three to 240.7±10 miligram/deciliter respectively. The impactbecameglaring from the seventh day and onwards. Group dealt withwithpopular drug glibenclamide (500 microgram/ /kilogram, orally) confirmedcomparableeffects and precipitatedgiantdiscount ($p<0.01$, n=6; one manner ANOVA with Dunnett'sposthoc test) in serum sugar **degree**, reducingimply blood glucose degree from 460.8±forty three to 206.2±50. Microgram/deciliter (Table 1).

Table 1: Action of daily intraperitoneal administration of *vincristine dose* andglibenclamide on serum sugar level of STZ produced sugar rodents.

S.NO	Groups	Dose (miligram /kilogram)	First days	fourth day s	seventh days	tenth day	fifteenth days	Twe nty fouth days
1	Diabetic control	0.4 milliliter	471.3±37	484.7±30	500.8±50	506±34	516.7±50	516.7 ±60
2	Normals gatherings control saline	0.4 milliliter	100 ±11	92.3±8	92.3±6	91.3±7	91.5 ±5	92.5± 6
3	Glibenclamide	500microgram/kilogram	460.8±43	300.7±45**	294.5±50**	248.8±53**	206.2±40**	206.2 ±50**
4	Vincristine	1.5 miligram/ kilogramip	477.7±18	476.3±22	345.7±20**	309.5±12**	244.3±12**	244.3 ±22**
5	Vincristine	3 miligram/ kilogramip	476.7±53	489.2±8	269.8±10** *	254.8±7***	240.1 ±10***	240.7 ±10***

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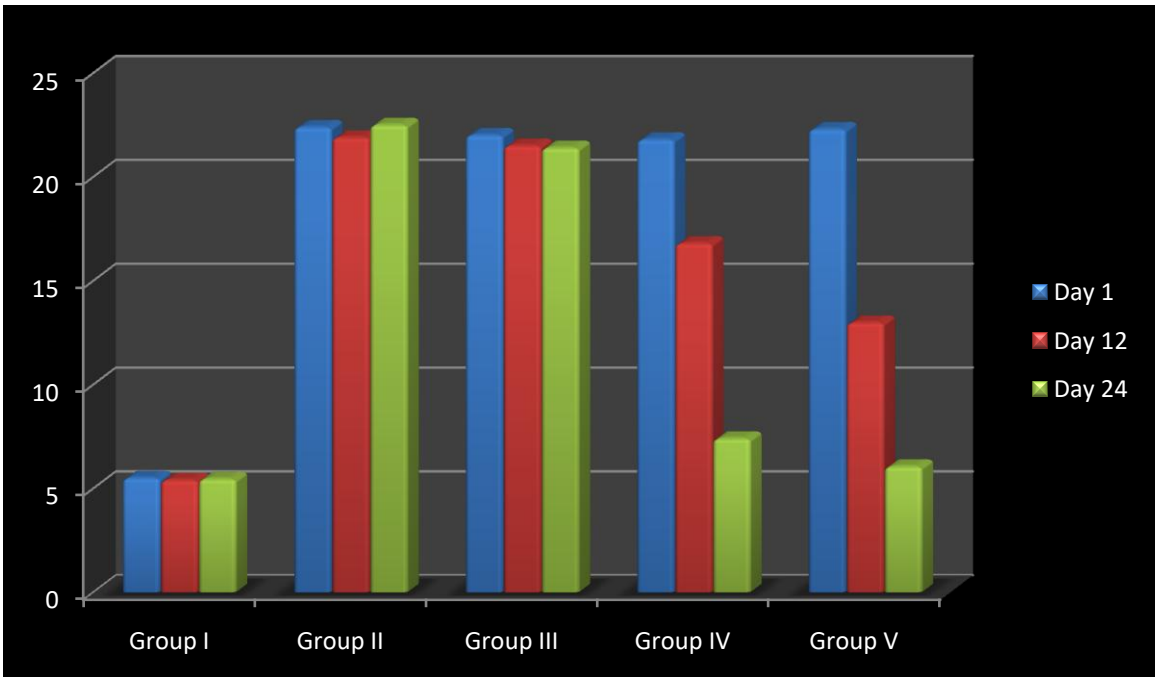

Figure:1Coumn effect showing of daily intraperitoneal administration of *vincristine dose* or glibenclamideon blood sugar level of Streptozotocin –produced diabetic rodents

Effects of vincristineon body weight in diabetic rats

The consequences of adjustments in frame weight of manage and experimental rats dealt withwith vincristine and glibenclamide are proven in desk 2. Streptozotocincaused diabetic rats produced significant (***p<0.001, n=6; Student's t test) loss in frame weight in comparison to regular rats at some point of the study (Table 4.3). In diabetic manage rodents, perseveredweight reductionturned intodetermineduntil the cease of the analysis (twenty fourth day's treatment). During this period, 13.8% discountof theirframe weight (Table 2) turned into recorded. Streptozotocin mediated frameweight lossturned into reversed via way of means of vincristine extract (1.5and 3miligram/kilogram b.w) . At the cease of fifteenth day's treatment, with vincristine 1.5 and 3 mg/kg inducedwill increase in frame weight via way of means ofnine.nine and 10.five percent respectively. (Table 2)

Table-2 Action of different dose of vincristine on body's weights inStreptozotocin produced sugars in rodents

Change in body's weights at days									
S.NO	**Treatments**	**Dose (mg/kg)**	**1st**	**4**	**7**	**10**	**15**	**24**	**% Change in body weight**

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1	Normal (Control)	0. 4 mililiter	153±0.5	155±9	165±0.9	170±0.9	178±3	178 ±4	
2	Diabetic (Control)	0.4 mililiter	152± 7	148 ±5*	145±5**	140±3**	133±4***	133 ±5***	-13.8
3	Glibenclamide	500microgram/kilogram	153±4	157±3*	160±6*	164±4**	168 ±5 **	169 ±6**	+11.1
4	Vincristine	1.5 miligram/kilogrami.p	152±3	155±5*	157±7*	160±5**	164±4**	165 ±5**	+9.9
5	Vincristine	3 miligram/kilogrami.p	154±4	155±6*	158±4*	162±3**	165±6**	165 ±7**	+10.5

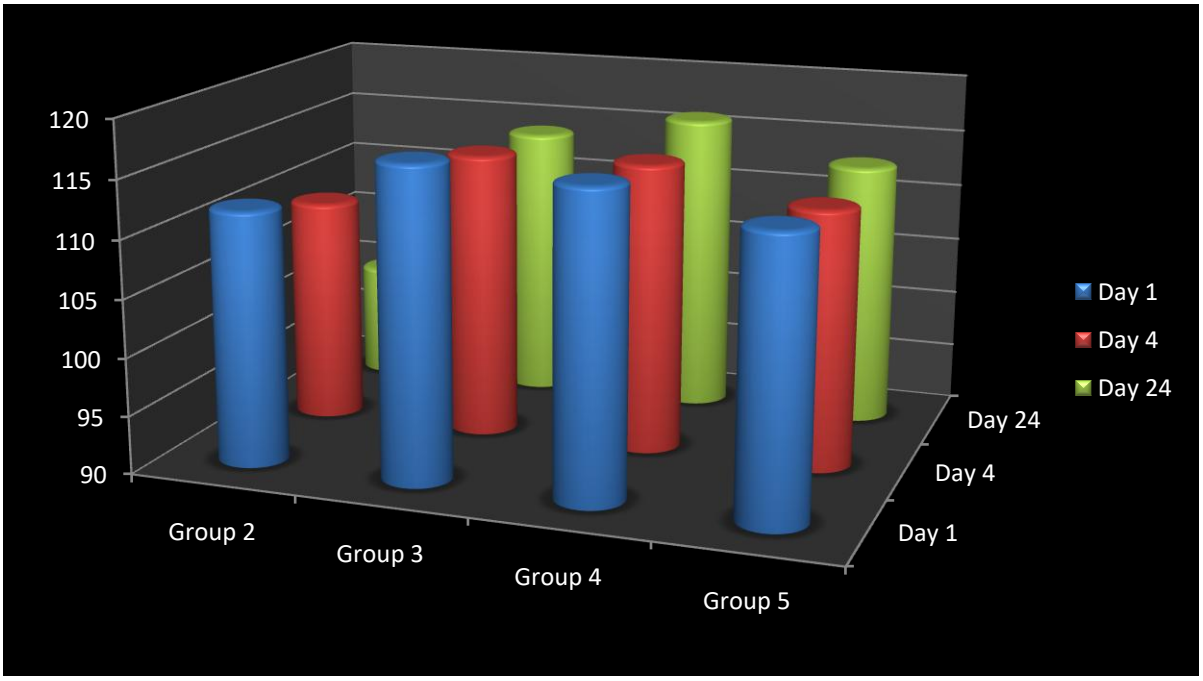

Figure:2 Column graph showing the effect of various dose of vincristine on body weight in STZ induced diabetic rats

Actions Of *vincristine* on lipid containing proteins profile in Streptozotocin-produced Diabetic Rodents

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The lipid profiles on top of things and investigational rodents are depicted in desk 3. In Streptozotocin - brought on diabetic manipulate rats, there has been a large (**p<0.01, n=6; Student's t test) growth in overalllow density containing lipid cholesterol, Triglyceride and low density containing lipid protien cholesterol'sas compared to everydaymanipulate. Additionally ,there has been a large diminish (*p<0.05, n=; Student's t tests) in high density containing lipid protien low density containing lipid protien cholesterol in sugar manipulate rodents in contrast to everydaymanipulate. Directing of the i.p injection vincristine methanolic extract (1.fiveand three milligram/kilogram) fraction for twenty-four days confirmed a large (**p<0.01,***p<0.001, n=six; one manner ANOVA with Dunnett'sposthoc tests) discount in overallldl cholesterol, Triglycerides and low density containing lipid protien cholesterol in contrast to diabetic manipulate rodents. The impactbecomeakin tothe same olddrug glibenclamide drug standard drug (500 microgram/kilogram). extended high density containing lipid protien low density containing lipid protien cholesterol in diabetic rat.

Table 3: Antihyperlipidemiceffect *of vincristine* different dosage in Steptozotocin -induced diabetic rodents

S.NO	**Preventive Doses (miligram/kilogram)**		**Total cholesterol (miligram/deciliter)**	**Triglyceride (miligram/deciliter)**	**High density containing lipd protein (miligram/deciliter))**	**Low density containing lipd protein (miligram/deciliter))**
1	Normal control	0.4 mililiter	120 ± 9.12	125 ± 8.80	34±2.2	81± 2.5
2	Diabetic Control	0.4 mililiter	185.3 ± 4.4**	169.0 ± 7.9**	30.2 ±2.4*	177.4±8.9**
3	Glibenclamide	500microgram/kilogram	137.7± 5.3**	128.3 ± 6.5**	39.1 ±2.3**	90.3± 3.5***
4	vincristine	1.5miligram/kilogram	144.2± 4.3**	138.5± 4.7**	37.5 ±3.1***	95.6± 3.2***
5	vincristine	3miligram/kilogram	140.5±7.5**	136.8±4.5**	35.6±5.5***	93.5±3.6***

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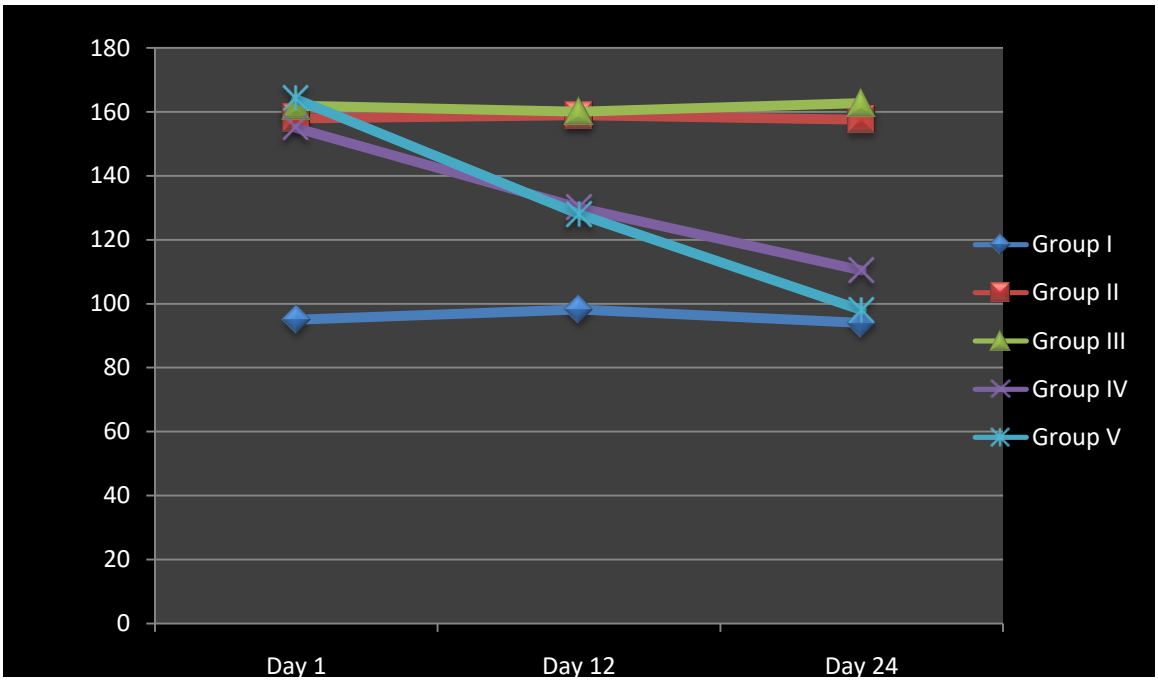

Figure-:3Line graph showing the antihyperlipidemiceffect *of vincristine* various fractions in STZ-induced diabetic rats

DISCUSSION

Notwithstanding the existence of recognized anti sugar prescription medications, naturalcapsules and arrangements are of tremendoushobby for the pharmacognosicalnetwork or are taken into consideration to be much lesspoisonous and unfastened from detrimental effects, than artificial agents . STZ is an antibiotic produced via way of means of Streptomyces chromogenic. In experimental animals, it reasons irreversible destruction of pancreatic beta cells, and is in the main used to result in diabetes mellitus in experimental animals via its poisonouseffects. The outcomes of the prevailingexaminesuggest that the vincristinedecreased blood glucose rangeswithinside thediabetogenic animal version with STZ (50 mg/kg). The vincristine injection fraction of established a giantdecreasing of blood glucose level (BGL). The antihyperglycemicimpact of vincristine can bebecause of prevention of unfastened radical formation brought onvia way of means of STZ. Elevated plasma overallldl cholesterol, triglycerides and LDL ldl cholesterol are the foremostdangerelements of cardiovascular diseases. Diabetic rats confirmedincreased plasma overallldl cholesterol, triglycerides and LDL IDL cholesterol. The vincristine (1.fiveand three mg/kg) decreased the lipid profile and prompteda discount in blood glucose level. STZ-brought on diabetes becamecharacterizedvia way of means ofextreme loss in frameweight. Reports have proven that the liver cells are irreversibly destroyed in STZ- brought on diabetic rats. These recordsshowed the

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opportunities that the foremostfeatureof those extracts is on protective in opposition to diabetes lipid decreasing, frame weight etc. (9, 10)

ACKNOWLEDGEMENTS

We are thankful to director, Advance Institute of biotech and Paramedical Sciences, for their kindly support for my work. We are grateful to the technical staff members of the Department of Pharmacology. We also thank the following persons: AnubhavDubey, Dakshina Gupta, Ashish Mishra, PallaviTiwari.

Author contribution

All author participated Equally.

Conflict of interest None

Funding None

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