

TROPICAL JOURNAL OF PHARMACEUTICAL AND LIFE SCIENCES

(An International Peer Reviewed Journal)

Journal homepage: <http://informativejournals.com/journal/index.php/tjpls>



EVALUATION OF ANTIDIABETIC ACTIVITY OF ETHANOLIC EXTRACT OF CITRULLUS COLOCYNTHIS

Kamal * and Rakesh Kumar Jat

Institute of Pharmacy,

Shri Jagdishprasad Jhabarmal Tibrewala University (SJJTU), Rajasthan, India

ABSTRACT

The plant which is selected for studies is *Citrullus colocynthis*. These plants are available in large quantities in desert area of Rajasthan and different region of the world. The pharmacological studies on diabetes mellitus, hyperlipidemia, fever, bacteria, wound healing activities and antioxidant activities of the plants have been tested and evaluated for various disease treatments like diabetes, fever, obesity and other many various disorders. The main focus is given against streptozocin induced diabetes treatment in albino rats and comparison is done with standard drug glibenclamide.

Keywords: Diabetes Mellitus, *Citrullus Colocynthis*, Streptozocin, Glibenclamide.

INTRODUCTION

Citrullus colocynthis is desert plant many grow in sandy regions of western Rajasthan particularly in rain season. It is similar to watermelon because fruit has the same shape. It is bitter in taste and mainly used for treatment of gastrointestinal problem in camel that is known as ship of desert. There are following important feature of *Citrullus colocynthis* given below. It is annual plant survive under extreme xeric conditions like high temp. *Colocynthis* is used with aloe in the treatment of wound healing as bandage. Fruit of *colocynthis* is used as laxative, diuretic and in insect bites. It was used by Arabic people to treat skin eruptions in camel¹.



Figure1: Ripe fruits and leaves of *Citrullus colocynthis*

*Corresponding Author:

Kamal,
Institute of Pharmacy,
Jagdishprasad Jhabarmal Tibrewala,
University, Jhunjhunu, Rajasthan, India

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Published by Informative Journals (Jadoun Science Publishing Group India)



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Western desert may have been portable ovens for roasting the fruit of colcynthis and used in preparation of breads. It is also used as emetic agent. It is rich in fat like linoleic acid and proteins. Seeds of colocynth have been used as food for Sahara desert people and the oil obtained from the seed can be used for preparation of soaps.

Chemical constituents:-The principle active composition of colocynth is linoleic acid, oleic acid, palmitic acid and stearic acid.

MATERIALS AND METHODS

Extraction is procedure of partitioning of restorative dynamic bit of creature tissues or plants utilizing specific solvents through standard techniques. Items in this way acquired from plants and creatures are moderately mind boggling blends of metabolites, which are in fluid or semisolid state or in event that dissolvable is expelled, at that point it might be in dry powder structure. They are expected for peroral or outside utility. These include various categories of mangement called as decoctions, imbuelements, tinctures, liquid concentrates, semi-solid concentrates or powder concentrate. During extraction, solvents diffuse into strong plant material and mixes with comparable extremity may solubilise in it. Air dried and coarsely powdered (50.00 gm). Leaves of *C. colocynthis* were extricated in ceaseless hot soxhlet extractor utilizing water. Concentrates were then thought to dryness under diminished tension, dried and they were safeguarded in cooler. Extraction is fundamental and starter step-in home-grown medication readiness and it acquires plant metabolites to solvents. Dissolvability of metabolites in chose dissolvable, temperature of extraction, powder size of plant materials and so on are different variables choosing effectiveness of extraction. Contingent on structure of particle, atom might be water dissolvable or water insoluble. Water insoluble mixes could be extricated utilizing certain natural solvents, for example, pentane, hexane, oil ether, chloroform, Ethyl acetic acid derivation, $(\text{CH}_3)_2\text{CO}$, ethanol and methanol. chose dissolvable ought to not influence or change or later first properties of mixes to be extricated and it ought to be effectively removable from framework. Decision of dissolvable is significant for extraction of plant material. There are different properties accessible for decent dissolvable. Properties of decent dissolvable in plant extractions may incorporates, low degree of poisonous quality, ease in dissipation at low warmth, advancement of quick and great physiologic assimilation of concentrate, additive activity of concentrate, powerlessness to make concentrate become perplexing or even separate concentrate. Different solvents utilized in extraction procedure are water, $(\text{CH}_3)_2\text{CO}$, alcohol, chloroform, ether, dichloromethane mineral acids and so on.

This strategy is broadly utilized in extraction of plant based unrefined medications. Soxhlet extraction is required, just where there is constrained dissolvability for ideal compound in dissolvable, and if polluting influence is insoluble in that dissolvable. On off chance that ideal compound has high dissolvability in dissolvable, at that point straightforward filtration system can be utilized to isolate compound from insoluble substance.

Soxhletor Apparatus

In year 1879 Franz Von Soxhlex developed instrument for extraction of phytochemical constituent that mechanical assembly called as Soxhlet extractor. This had been started first for intention of extraction of fat from storage substance. Be that as it may, Soxhlet extractor isn't restricted to extract of fats. Ordinarily, Extraction by soxhlet was needed there ideal substance had restriction dissolvability in solvable, and contamination was not soluble in that soluble. On off chance that ideal compound has noteworthy dissolvability in dissolvable, at that point basic filtration can be utilized to isolate compound from insoluble substance.

Powder of compound is set inside thimble produced using thick channel paper, which is stacked into fundamental office of Soxhlet apparatus. Soxhlet apparatus is put onto flagon consisting of extract dissolvable. Soxhlet is then outfitted with condenser.

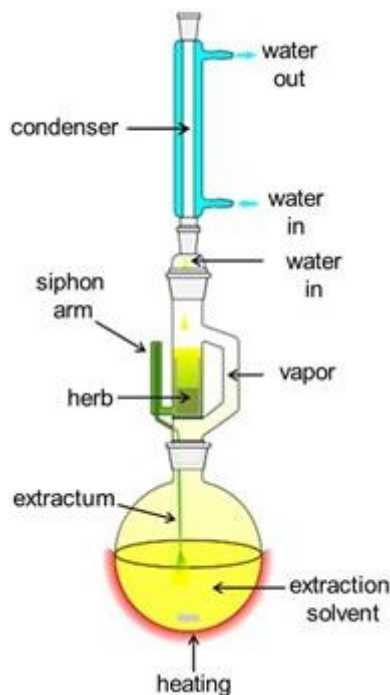


Fig. 2: Soxhletor apparatus

Soxhlet chamber was practically full at that point, chamber is naturally purged by siphon side arm, with dissolvable getting down to refining cup. This cycle was permitted to rehash 03 days. During each cycle, segment of non un-predictable substance disintegrates in soluble. This apparatus is used for recycling of solvent with help of warming with heating mental in the bottom of apparatus. Complete removal of active constituent in the concerned solvent is possible with this procedure in this apparatus.

1. Removal of move balance by over and again getting crisp dissolvable to contact with strong grid.
2. Keeping up moderately high extraction temperature with heat from distil lat particle cup.
3. No filtration of concentrate is required.

Planning of standard stock arrangement of watery leaf concentrate of *Citrullus colocynthis*

The substance of 50.00 mg of *Citrullus colocynthis* separate, was gathered, gauged and moved into 10.00 ml standard cup and removed with methanol for 60.00 min. resultant concentrate was sifted and filtrate was dissipated to dryness. dried concentrate got was broken down in 5.00 ml of methanol and arrangement was sifted through Whatmann channel paper. Filtrate was gathered and utilized for additional investigations.

Alloxan Induced Diabetic Model

Alloxan (2, 4, 5, 6-tetraoxypyrimidine; 2, 4, 5, 6-pyrimidinetetrone) is oxygenated pyrimidine subordinate. It is accessible as alloxan hydrate in watery game plan. Alloxan in any case called 5 – Oxo-barbaturic and meso-oxylurea destructive contain sub-nuclear condition $C_4N_2O_4H_2$, Molecular weight 141.96 gram per mole also uninhibitedly dissolvable in H_2O . it surprisingly collects in β cells throughout take-up by method for its decreasing thing, dialuric hazardous savage improvement of alloxan is begun by free radicals bound right now. One examination endorses that alloxan doesn't achieve diabetes in individuals.

Mechanism of Action

Alloxan have 02 unquestionable over top impacts. It especially checks glucose insulin discharge through explicit square or glucokinase, sugar sensor of β cell, this induces condition of hormone-ward diabetic within its capacity to impact R.O.S. approach, satisfying explicit wrecking of B-cells. These 02 impacts can be given to explicit compound possessions of alloxan, critical region being specific cell take-up gathering of alloxan by beta cell (Szkudelski, 2001).

Chemical Names: Alloxan; 2,4,5,6 (1H, 3H)- Pyrimidinetetrone; 50-71-5; Mesoxalylurea; Mesoxalylcarbamide; ALLOXANE.

Atomic Formula: C₄H₂N₂O₄

Atomic Weight: 142.07 g/mol

Medication Information: Therapeutic use FDA, UNII

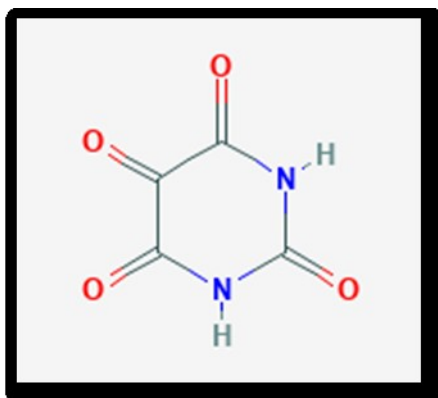


Fig. 3: Structure of alloxan

Trial Animals

The pale skinned person rodents (0.150-0.180 Kg) were secured from Karavali school of drug store, Mangalore, India. creatures were housed in gathering of 06 rodents for each enclosure and kept up under standard research facility condition at 24.00± 2.00°C in light controlled room (12.0 h dull/12.0 h light) and were given business pellet diet, filtered drinking water not indispensable. Investigation was affirmed by IAEC comprised with end goal of CPCSEA Govt of India.

Experimental design

The rodents were partitioned into six gatherings of 06 rodents each.

Gathering I – Normal control rodents

Gathering II – Alloxan treated control rodents (120.00 mg/kg b.wt)

Gathering III – Alloxan + standard medication Glibenclamide (10.00 mg/kg b.wt)

Gathering IV – alloxan + fluid leaf concentrate of *C. colocynthis* (100.00 mg/kg b.wt)

Gathering V–alloxan + fluid leaf concentrate of *C. colocynthis* (250.00 mg/kg b.wt)

Gathering VI-Alloxan + watery leaf concentrate of *C. colocynthis* (500.00 mg/kg b.wt).

Induction of diabetes

Type II diabetes was initiated to pale skinned person rodents by solitary intraperitoneal (i.p) infusion of alloxan monohydrate (120.00 mg/kg b.wt) in clean typical saline (00.90%). diabetic state was resolved following 3.00 days of alloxination by high blood glucose level and loss of body weight. Toward finish of tenth day for intense treatment and 30th day's sub intense treatment, blood glucose level was evaluated by one touch glucometer and rodents were relinquished under chloroform sedation.

Streptozotocin Induced Diabetic Model²

Streptozotocin is genuinely happening structured that is predominantly perilous to insulin passing on B-cells of pancreas in all around bleeding edge animal. It is used as bit of solution for cuing positive tumor of islet and utilized piece of strong assessment to pass on creature model for class 1 diabetes and has molecular weight of 264.95 gram/mol. It is assessment is H₁₅C₈O₇N₃.

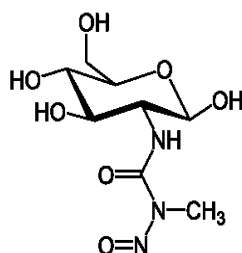


Fig. 4: Structure of STZ

STZ was lasting diabetic inciting medicament. This was integrated with strain of dirt organism *S. achromogene* (gram +tive bacteria) along wide range of anti-bacterial characteristics. STZ is bizarre amino-glycoside consisting of nitroso-amino bunch found in 1984 as anti-toxin, presently promoted as conventional medication. STZ has been broadly utilized to actuate diabetic in abino wistar rat with restraint of beta cell O - GlcNAcase (Vivek K. 2010).

Experimental Animals

Creature Male wistar rodents between 12.00 multi week old enough and weighing 0.250-0.300 Kg were acquired from creature place of Pharmacy School of drug store Jaipur, India. Creatures had been maitianed under environmental factors along taken care of along rat H₂O and diet not indispensable. Diabetic conditions had been actuated in rodents by intra-venous infusion of streptozotocin at portion of 49.95 milligram per kilogram of weight, disintegrated in 00.10M virus citric acid ester cushion (pH = 04.50) (Sanchheti et al;, 2011). Blood sugar quantity had been estimated utilizing G.O.D. and P.O.D. (Kit spinrreact). Blood tests had been pulled back from retroorbital plexuses along with light general ether. Exploratory convention typical rodents and those with hyperglycemia (blood glucose 0.200-0.360 g/dl) were separated into 06 gatherings of 06 creatures each and treated by per oral. Blood tests and body weight were estimated at week after week interims on days 0.0, 04, 07, and 10.0, till finish of research. Blood sugar quantity had been estimated utilizing G.O.D. and P.O.D. (Kit spinrreact) (Trinder, 1996). Body weight additionally saw during investigation time.

Test Plan

The rodents were isolated into 06 gatherings of 06 rodents each.

Gathering I – Normal control rodents

Gathering II – STZ treated control rodents (120.00 mg/kg b.wt)

Gathering III – STZ + standard medication Glibenclamide (5.00 mg/kg b.wt)

Gathering IV – STZ + fluid leaf concentrate of *C. colocynthis* (100.00 mg/kg b.wt)

Gathering V–STZ + fluid leaf concentrate of *C. colocynthis* (250.00 mg/kg b.wt)

Gathering VI-STZ + fluid leaf concentrate of *C. colocynthis* (500.00 mg/kg b.wt)

Acute treatment was performed for 10.00 days. Furthermore, sub adorable treatment was done at 01 month. Toward finish of 30th day's treatment, blood glucose level was assessed by one touch glucometer and rodents were yielded under chloroform sedation. Blood was gathered and centrifuged at 3000.00 rpm for 20.00 minutes to isolate serum. Liver was expelled and washed with super cold typical saline (00.90 %) to evacuate blood. Around 1.00 g of liver tissue was homogenized utilizing 00.10 M Tris – Hcl cushion at pH 04.70 and supernatant was isolated. Serum and supernatant were utilized to break down natural parameters inside 01 day of penance. Above strategy are followed for sub intense treatment gathering. For sub intense gathering blood tests were gathered on 30th day of treatment.

Animals

Rodents were acquired from two sources. Storage eating regimen had given according to standards which having accompanying rate structure as indicated by producer: fiber 4.11, lipid 4.50, protein 23.94, starch 44.00, debris 11.00, and dampness 10.00. To prohibit chance of variety along sex in sugar take-up with stomach, rodents of male sex had been utilized along 3 special cases. Maximum rodents weighted somewhere in range of 100.00 and 200.00 gm. when relinquished. More youthful creatures had stomachs too little to even think about yielding ideal number of tests; bigger creatures were once in while utilized, however those gauging more than 300.00.

The creatures had been further administered storage eating routine, along 1 percent NaCl answer for taking water, tlil relinquished. Adrenal-ectomy of diabetes rodents had been trailed with down of glucose of feed creatures from 299.96 to 799.98 to around 199.96 to 399.98 %mg; the diabetes adrenal-ectomized rodents

couldn't have securely fast upto 15.98 to 19.98 hrs, as these would in general kick bucket of hypo-glycemia. On that record, fast time of 06 hrs had been utilized; right now glucose tumbled to ordinary qualities or underneath, as opposed to glucose of in excess of 300.00 mg. percent after quick of 16.00-20.00 hours in similar diabetic creatures before adrenal-ectomy. Solution medium (Krebs 1932) had been utilized in all analyses. It had been picked on account of their comparability for extracellular liquid as for ionic substance.

Experimental Protocol

In all analyses, with exception of those explicitly noticed, gas stage was 95.00 % oxygen-5.00 % CO₂, providing underlying pH of 07.40 to media. Gemill (1941) found that glucose usage by rodent stomach had been more along 299 or 499 milligram. percent of sugar in media than with 199.98 %mg; these additionally obtained that supreme increment in sugar use created with hormone had been fairly bigger at 299.97 or 499.95 % milligram. than at 199.94 % milligram.

For current examination, two centralizations of glucose were attempted, 100 and 200 mg. percent. In spite of fact that pace of glucose usage and impact of insulin would in general be to some degree more at 199.98 than at 99.99 milligram. Percent, less focus had been picked to majority of investigations so as to look at paces of glucose use at substrate fixation relating to typical glucose level. To permit incitement by insulin to be shown obviously, heaviness of stomach test was constrained to around 30.00 mg. with goal that sugar focus in medium would not fall beneath 50.00 %mg toward finish of hatching time frame. Moreover, couples of examinations were run at 200.00 %mg. Every 50.00% of stomach was then sliced long way to yield 02 pieces further again sub-divided when fundamental. Every piece had been smudged independently, burdened torsion parity, and moved to cold medium have test tube or in little round base tube shaped vessel arranged for reason via close one finish of 00.50 m. lengthing of 15.99 millimeter. Media was recently set in vessels by methods for Lang-Levy miniaturized scale pipette; smaller scale pipettes conveying 00.09 to 00.116 ml. were utilized for inspecting toward finish of examination. Vessels containing tissue and media had been further connected to mano-meters, equilized along air stage, put with shower at 36.95, then agitated upto 2.00 hrs to 95.96 cycles for every moment. Toward finish of 02 hour time frame, test tubes had been evacuated, tighten with stopper, and colded with ice H₂O. For investigation of lingering sugar in media, copy 00.10 - 0.115 milliliter. Aliquot had been dropped out 01.50 ml. of aqua then hastened along 00.20 milliliter. Every one of Ba(OH)₂ along ZnSO₄; 01.00 milliliter. tests of filtrating fluid had been investigated by Nelson's strategy. Tests to first media had been helped throughout investigation simultaneously, further then sugar usage had been controlled with contrast.

So as for evaluating criticalness with distinctions for sugar usage within stomachs along different sorts with creatures, 02 outcomes were broke down measurably by standard techniques. estimations of P had been received with Fisher t table; as indicated by this technique for articulation, estimation of P = 00.01 implies that distinction watched would happen by chance just single time in hundred preliminaries, and so forth.

Right now portion of 120.00 mg/kg body weight alloxan monohydrates was infused by intraperitoneal course to instigated diabetes in tentatively fasted rodents. 2.00% glucose arrangement was given to creature rather than ordinary water to drink. For scarcely any days till continue hypoglycemia was exist. Blood glucose level up to 300.00 mg/dl and at very least 180.00 mg/dl after glucose admission is as further analysis creature

Before that rudimentary test was accomplished for fluid leaf concentrate of *C. colocynthis* on creature for hypoglycemic movement of various portion to choose more strong portion which was utilized in ensuing test examines.

The impact of fluid leaves concentrate of *C. colocynthis*, and alloxan prompted diabetes medicines, were seen on: body weight, oral glucose resistance test, serum insulin, blood glycerated haemoglobin rate, liver glycogen substance, and serum ALT and AST movement, and lipid profile. Fringe glucose take-up by rodent hemi stomach strategy insulin discharge from disconnected islet of Langerhans in vitro was

performed and intestinal glucose retention *in situ* was evaluated. rate concentrate likewise incorporates histopathological changes in pancreases of ordinary, diabetic control and diabetic treated rodents³.

Pale skinned person rodents of either sex weighing 0.180-0.200 Kg fasted medium-term was utilized for examination. After test time of about month all fasted creature was tried for oral glucose resilience test. Following 01 day of rodents are yielded by execution and blood test was gathered from rodents pancreases was immediately isolated from relinquished creature. New liver example was utilized for glycogen content assurance. After execution and stomach was taken out rapidly evading injury and isolated into equal parts. Hemi stomach was washed in chilled tyrode arrangement with no sugar to expel all blood coagulations also will be set within little cone shaped jar containing 2.00 ml tyrode arrangement with 2.00% glucose and brooded for 30.00 minutes at 37 °C. (Saba MC, 2000)

a) For glucose take-up:

The hemidiaphragms was brooded for 30.00 min at 37°C in environment at 95% oxygen and 5.00 %carbon dioxide with shaking at 140.00 cycles every moment. For sets of trials was performed. Hemi stomachs were presented to:

1. Tyrode arrangement with 2.00 % glucose. This gathering will fill in as control.
2. Tyrode arrangement with 2.00 % glucose + insulin(00.25I.U/ml) standard
3. Tyrode arrangement with 2.00 % glucose + leaves extracts(different portion levels) filled in as test
4. Tyrode arrangement with 2.00 % glucose + insulin + leave remove

Hemi-stomachs had been obtained with sugar substance to hatched media will be estimated by glucose oxidase strategy. Glucose take-up will be determined as distinction among starting and last glucose content in brooding medium.

b) For glycogen content:

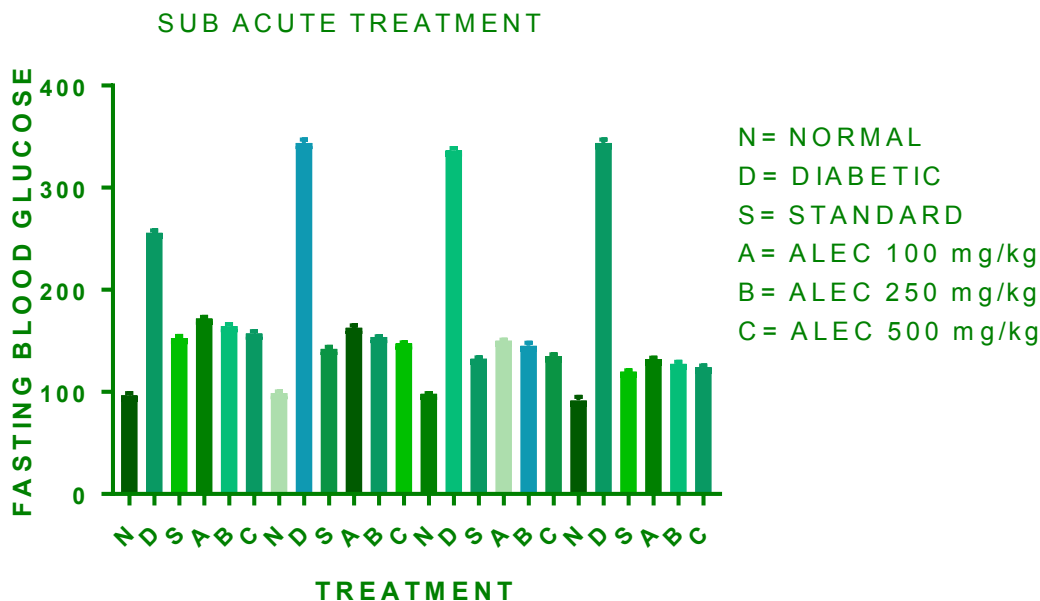
The hemi stomach was hatched in tyrode arrangement with glucose (2.00 %) in comparable route concerning glucose take-up. Just time will be stretched out to 90.00 minutes. Following brooding hemi stomachs will be flushed for 10-15 sec in 00.90 % NaCl at 0°C to wash off outside glucose and to stop chemical action. It was blotched, solidified on dry ice and glycogen substance of tissue was estimated by anthrone technique for carroll et al. glycogen substance will be communicated in microgram/milligram of tissue⁴.

RESULT AND DISCUSSION

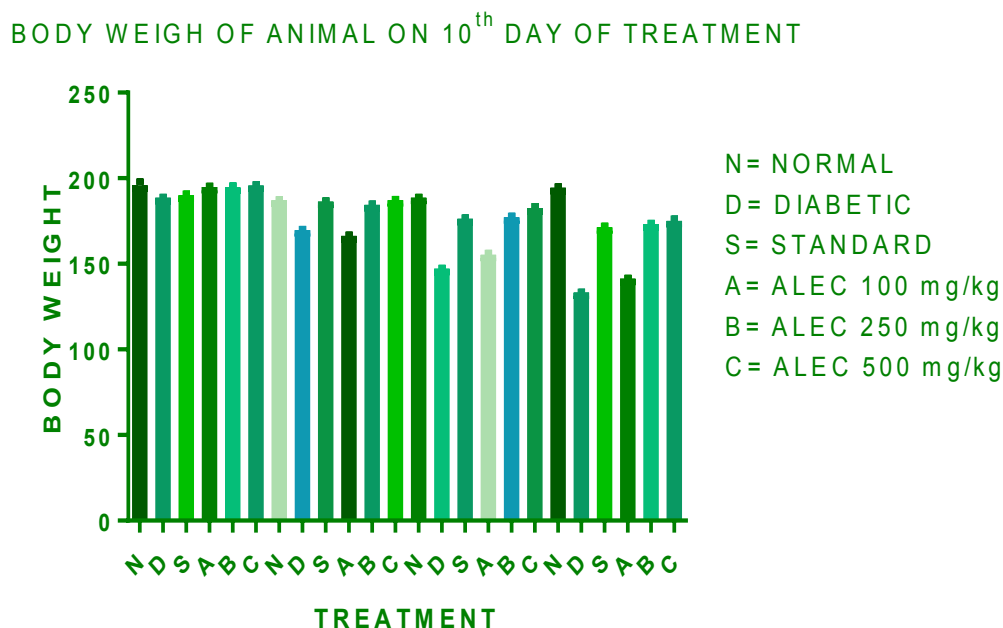
Alloxan Induced Diabetic Model

Impact of watery leaves concentrate of *C. colocynthis* (CCEC) on fasting blood glucose level in diabetes rodent. Watery leaves concentrate of *C. colocynthis* (CCEC) was exposed to hostile to diabetic action in rodents where alloxan monohydrates was utilized as portion of 120.00 mg/kg in intra peritoneal portion as diabetogenic specialist to acquainted diabetic with test rodents. Alloxan has been tentatively utilized diabetes instigating operator because of particular pulverization of insulin creating pancreatic beta cells.

In sub intense treatment bunch blood glucose levels are seen on 14.00th, 21.00th and 30.00th day present treatment compare on typical control in diabetic control checked expanded blood glucose level was watched. CCEC portion of 100.00 mg/kg caused decrease in blood glucose level however outcomes were found measurably non significant. Fluid leaves concentrate of *C. colocynthis* at portion 250.00 mg/kg cause decrease in blood glucose level however contrast with 500.00 mg/kg 250.00 was less yet both are noteworthy. On 14.00th 21.00th and 30.00th day post treatment with CCEC produce portion reliance against hyperglycemic action. At portion of 100.00 mg/kg was non importance contrast and reference standard medications is glibenclamide. Antidiabetic action was discovered portion subordinate 500.00 mg/kg was watched progressively noteworthy. And 100.00 mg/kg was discovered less successful. Glibenclamide utilized as standard reference medicate.

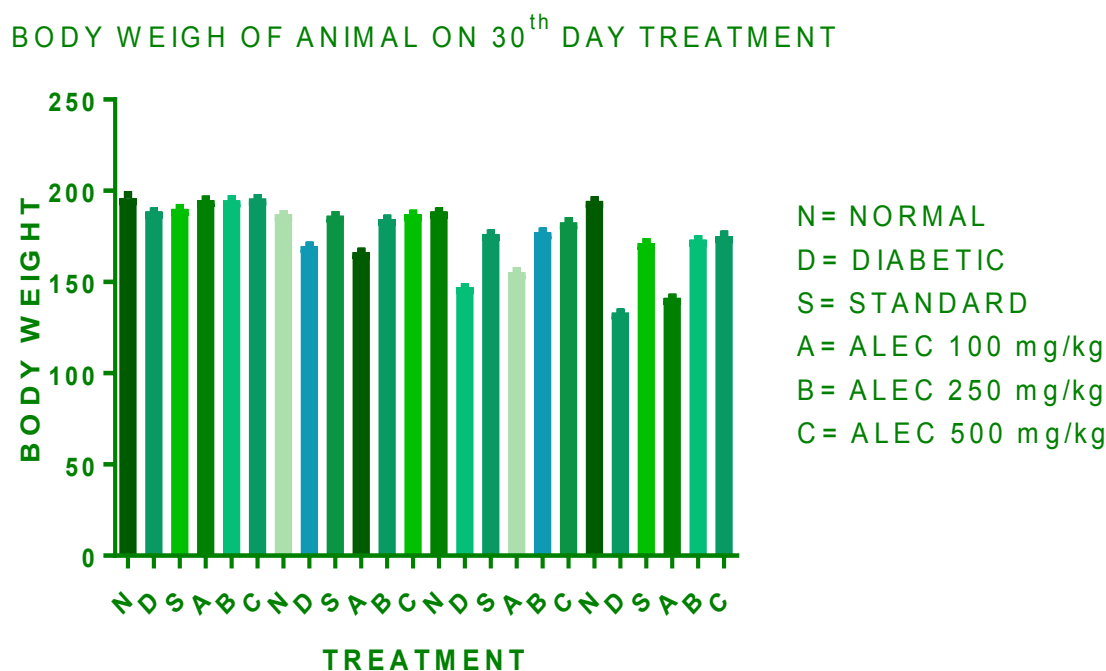


Graph: 1- Effect of CCEC on fasting blood glucose level on sub acute alloxan treatment group



Graph: 2- Effect of CCEC on body weight in acute alloxan treatment group

Effect of gel concentrate of *C. colocynthis* on body weight in alloxan actuated diabetes rodents sub intense treatment. During multi month treatment of creature in diabetic control body weight of creature was discovered fundamentally diminished where in ordinary benchmark group's body weight was discovered stable. Alloxan interceded body weight decrease was noteworthy turned around by fluid concentrate of watery *C. colocynthis* in portion subordinate design. Impact of CCEC at portion of 100.00 mg/kg on body weight was found factually not noteworthy. Where 250.00 mg/kg and 500.00 mg/kg was discovered portion dependence criticalness on body weight of creatures⁵.



Graph: 3- Effect of CCEC on body weight in sub acute alloxan treatment group

Impact fluid concentrate of *C. colocynthis* on biochemical parameters Post treatment with CCEC for time of 10.00 days in treatment bunches watched decreased in Serum urea, serum creatinine and serum cholesterol levels when contrast with diabetic control, while serum protein level was expanded altogether when contrast with diabetic gathering. Anyway CCEC portion 100.00 mg/kg neglected to turn around adjusted biochemical parameters. In any case, 250.00 mg/kg and 500.00 mg/kg watched portion depend decrease was found in lipid parameters contrast and diabetic control.

In intense treatment bunches biochemical parameters are assessed on tenth day post treatment with CCEC at portion of 100.00, 250.00 and 500.00 mg/kg. on 10.00th day serum urea was recorded in ordinary benchmark groups as 26.68±01.63 mg/dl diabetic control 58.00±01.41 mg/dl and standard medications treatment bunches was 28.34±01.03 mg/dl and CCEC treatment bunches were 55.34±01.63 mg/dl, 37.00±01.41 mg/dl and 32.17±01.83 mg/dl for 100.00, 250.00 and 500.00 mg/kg individually. From this information we saw in diabetic benchmark groups serum urea was more which are turned around by CCEC. In CCEC treatment bunches most extreme decrease was seen in 500.00 mg/kg followed by 250.00 mg/kg. 100.00 mg/kg likewise decreased serum urea however it was not importance. While glibenclimide utilized as standard.

In intense treatment bunches biochemical parameters are assessed on tenth day post treatment with CCEC at portion of 100.00, 250.00 and 500.00 mg/kg. on 10.00th day serum creatinine was recorded in typical benchmark groups 00.89±00.02 mg/dl diabetic control 00.98±00.02 mg/dl and standard medications treatment bunches was 00.56±00.01 mg/dl and CCEC treatment bunches were 00.99±00.10 mg/dl, 00.67±0.01 and 00.56±00.003 mg/dl for 100.00, 250.00 and 500.00 mg/kg individually. From this information we watched serum creatinine level was stamped expanded in diabetic benchmark group contrast and normal control gathering. huge reduction of serum creatine was seen in treatment bunch treated with CCEC 250.00 mg/kg and 500.00 mg/kg body weight. CCEC portion of 100.00 mg/kg likewise caused decrease in serum creatinine level yet outcomes were found measurably non critical for treatment period 10.00 days. CCEC was discovered portion depend decrease of serum creatinine decrease. Fluid

leaves concentrate of *C. colocynthis* at portion 100.00 mg/kg was discovered less compelling than reference standard medications glibenclamide.

CCEC at portion of 100.00, 250.00 and 500.00 mg/kg, On 10.00th day post treatment. Serum cholesterol levels of all gatherings are recorded. serum cholesterol levels were typical benchmark groups 105.80±16.12 mg/dl diabetic control 175.00±14.12 mg/dl and standard medications treatment bunches was 112.00±03.84 mg/dl and CCEC treatment bunches were 170.2±5.26 mg/dl, 141.60±01.21 mg/dl and 126.00±02.50 mg/dl for 100.00, 250.00 and 500.00 mg/kg separately. From this information we watched stamped expanded in serum cholesterol level in diabetic control contrast with ordinary control rodent. From this information we watched serum creatinine level was checked expanded in diabetic benchmark group contrast and normal control gathering. huge reduction of serum creatine was seen in treatment bunch treated with CCEC 250.00 mg/kg and 500.00 mg/kg body weight. CCEC portion of 100.00 mg/kg additionally caused decrease in serum creatinine level yet outcomes were found factually non noteworthy for treatment period multi month. CCEC was discovered portion depend decrease of serum creatinine decrease. Fluid leaves concentrate of *C. colocynthis* at portion 100.00 mg/kg was discovered less viable than reference standard medications glibenclamide.

In intense treatment bunches biochemical parameters are assessed on 10.00th day post treatment with CCEC at portion of 100.00, 250.00 and 500.00 mg/kg. on tenth day serum protein was recorded in ordinary benchmark groups as 05.16±00.75 mg/dl diabetic control 02.83±00.75 mg/dl and standard medications treatment bunches was 05.50±01.04 mg/dl and CCEC treatment bunches were 04.16±00.40 mg/dl, 04.66±00.81 and 05.16±01.16 mg/dl for 100.00, 250.00 and 500.00 mg/kg individually. From this information we saw in diabetic benchmark groups serum protein was less contrast with control, which were turned around by CCEC. In CCEC treatment bunches most extreme recover was seen in 500.00 mg/kg followed by 250.00 mg/kg. 100.00 mg/kg likewise recover serum protein however it was not criticalness. While glibenclimide utilized as standard medications.

In sub intense treatment bunches biochemical parameters are assessed on 30.00th day post treatment with CCEC at portion of 100.00, 250.00 and 500.00 mg/kg. on 10.00th day serum protein was recorded in ordinary benchmark groups as 05.33±00.81 mg/dl diabetic control 03.16±00.73 mg/dl and standard medications treatment bunches was 05.83±00.75 mg/dl and CCEC treatment bunches were 04.16±00.75 mg/dl, 04.83±00.75 and 05.33±01.05 mg/dl for 100.00, 250.00 and 500.00 mg/kg separately. From this information we saw in diabetic benchmark groups serum protein was less contrast with control, which were turned around by CCEC. In CCEC treatment bunches most extreme recover was seen in 500.00 mg/kg followed by 250.00 mg/kg. 100.00 mg/kg additionally recapture serum protein however it was not noteworthiness. While glibenclimide utilized as standard medications.

In sub intense treatment bunches biochemical parameters are assessed on 30.00th day post treatment with CCEC at portion of 100.00, 250.00 and 500.00 mg/kg. on 30.00th day serum urea was recorded in ordinary benchmark groups as 26.84±00.98 mg/dl diabetic control 59.69±01.86 mg/dl and standard medications treatment bunches was 26.00±02.89 mg/dl and CCEC treatment bunches were 56.52±01.04 mg/dl, 37.32±01.21 mg/dl and 30.52±01.04 mg/dl for 100.00, 250.00 and 500.00 mg/kg separately. From this information we watched serum urea level was stamped expanded in diabetic benchmark group contrast and normal control gathering. critical reduction of serum urea was seen in treatment bunch treated with CCEC 250.00 mg/kg and 500.00 mg/kg body weight. CCEC portion of 100.00 mg/kg additionally caused decrease in serum urea level yet outcomes were found measurably non huge for treatment period multi month . CCEC was discovered portion depend decrease of serum urea. Fluid leaves concentrate of *C. colocynthis*

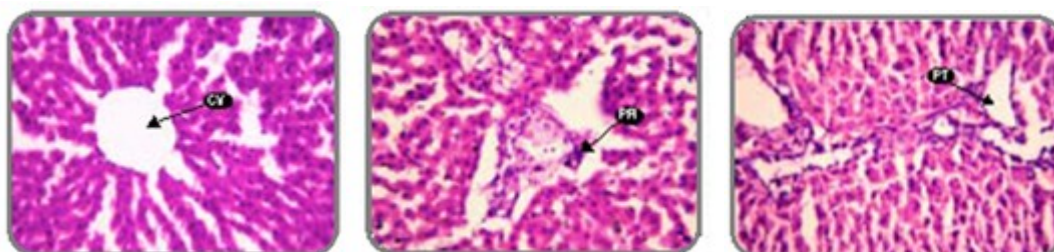
at portion 100.00 mg/kg was discovered less compelling than reference standard medications glibenclamide.

In sub intense treatment bunches biochemical parameters are assessed on 30.00th day post treatment with CCEC at portion of 100.00, 250.00 and 500.00 mg/kg. on 30.00th day serum creatinine was recorded in typical benchmark groups was 00.90 ± 00.01 mg/dl diabetic control 00.99 ± 00.02 mg/dl and standard medications treatment bunches was 00.55 ± 00.01 mg/dl and CCEC treatment bunches were 00.99 ± 00.10 mg/dl, 00.67 ± 00.01 and 00.55 ± 00.01 mg/dl for 100.00, 250.00 and 500.00 mg/kg separately. From this information we watched checked expanded in serum creatinine level in diabetic control contrast with typical control rodent. Fluid leaves concentrate of *C. colocynthis* at portion 250.00 and 500.00 mg/kg showed portion subordinate huge decrease was watched. CCEC portion of 100.00 mg/kg likewise caused decrease in serum creatinine level yet outcomes were found measurably non huge. Watery leaves concentrate of *C. colocynthis* at portion 100.00 mg/kg was discovered less successful than reference standard medications glibenclamide.

CCEC at portion of 100.00, 250.00 and 500.00 mg/kg, on 30.00th day post treatment. Serum cholesterol levels of all gatherings are recorded. serum cholesterol levels were ordinary benchmark groups was 107.70 ± 01.21 mg/dl diabetic control 178.50 ± 01.04 mg/dl and standard medications treatment bunches was 111.30 ± 02.40 mg/dl and CCEC treatment bunches were 171.20 ± 01.03 mg/dl, 145.80 ± 02.92 mg/dl and 118.80 ± 03.86 mg/dl for 100.00, 250.00 and 500.00 mg/kg separately. From this information we watched stamped expanded in serum cholesterol level in diabetic control contrast with ordinary control rodent. From this information we watched serum cholesterol level was stamped expanded in diabetic benchmark group contrast and normal control gathering. Noteworthy reduction of serum cholesterol was seen in treatment bunch treated with CCEC 250.00 mg/kg and 500.00 mg/kg body weight. CCEC portion of 100.00 mg/kg likewise caused decrease in serum cholesterol level yet outcomes were found factually non noteworthy for treatment period 30.00 days. CCEC was discovered portion depend decrease of serum cholesterol decrease. Watery leaves concentrate of *C. colocynthis* at portion 100.00 mg/kg was discovered less viable than reference standard medications glibenclamide.

HISTOPATHOLOGICAL EXAMINATION

Histopathology of liver, kidney and pancreas was studied in treatment animal with aqueous leaves extract of *C. colocynthis*. For that specific tissue are taken stained and observed in microscope. In observation of liver tissue it was seen that In normal tissue section in treatment groups shows sinusoidal cards of hepatocytes with central vein and portal tracts. portal tracts show portal triad with portal vein, hepatic artery and bile duct, whereas diabetic rat tissue section shows distortion in arrangement of cells around central vein, peri portal fatty infiltration with focal necrosis of hepatocytes. aqueous leaves extract of *C. colocynthis* (100.00, 250.00 and 500.00 mg/kg body weight) treated brought back cellular arrangement around central vein and reduced necrosis. Also it helped to bring blood vessels to normal condition. group V and VI means dose of 250.00 and 500.00 mg/kg showed significant change of liver, when compared with control group.



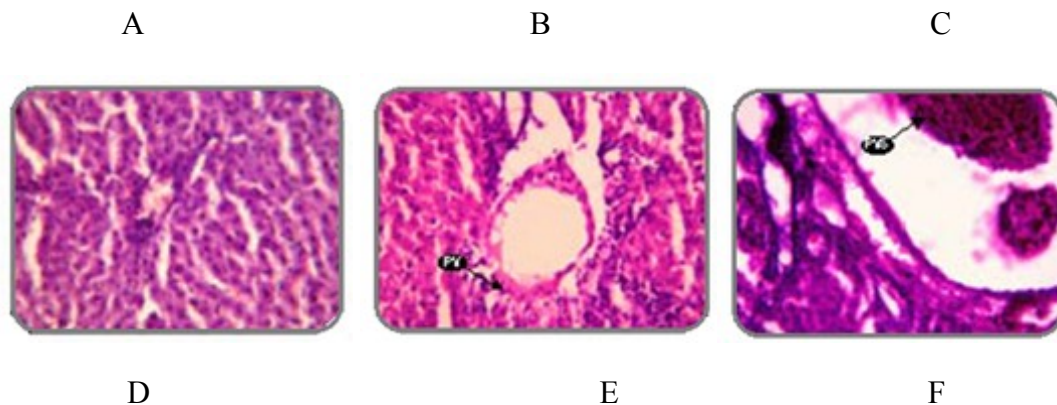


Fig: 5-Histopathology of liver in alloxan induced diabetic animal after treatment with CCEC of different dose

Histopathological Changes in Liver of Control and Experimental rats. A. Group I - Normal liver showing CV with radiating cords of hepatocytes; B. Group II – treated with alloxan Diabetic liver shows periportal fatty infiltration (PFI) with focal fat necrosis; C. Group III treated with CCEC 100mg/kg - Shows normal portal tract (PT); D. Group IV Portal track showing normal features; E. Group V - Congested and edematous PV with mild haemorrhage; F. Group VI -Portal vein shows haemorrhage in lumen in PVS

Kidney sections of diabetic rat showed tubular damage, proteinuria and haemorrhage. Haemorrhage is seen with in Bowman’s space due to glomerular damage (diabetic control). In aqueous leaves extract of *C. colocynthis* (250.00 and 500.00 mg / kg body weight) treated diabetic kidney, damaged capillary loops with increase in thickness of wall, glomeruli and tubules without proteinuria and haemorrhage. Group V and VI did altered structure of kidney which are deform in alloxan induced diabetic group, when compared with group I.

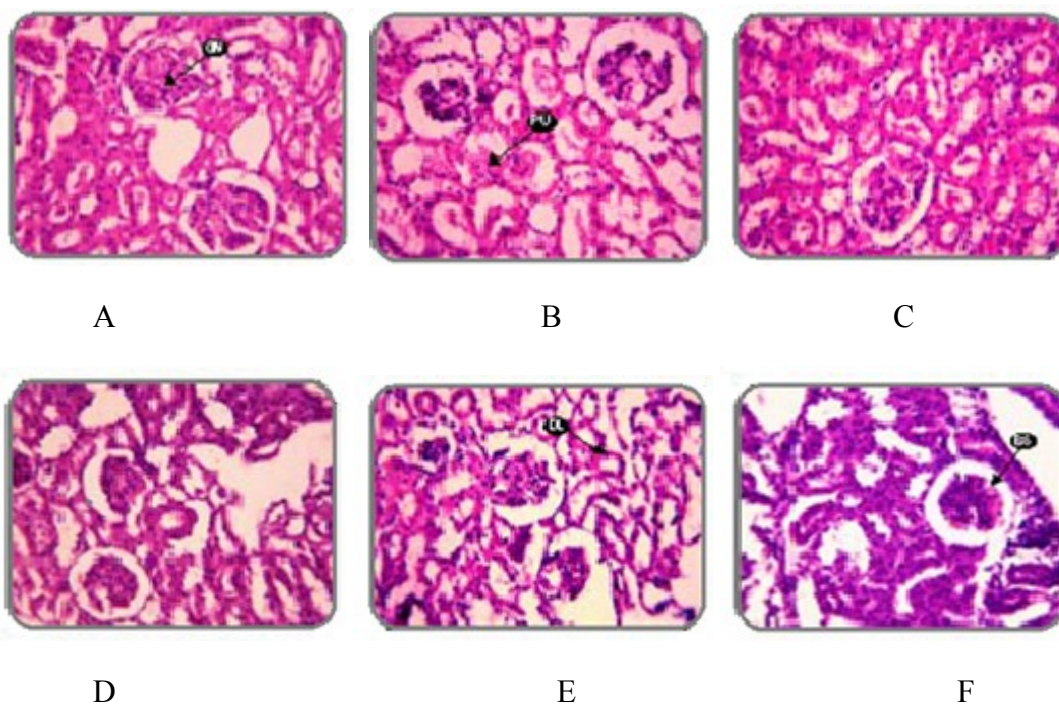


Fig: 6-Histopathology of Kidney in alloxan induced diabetic animal after treatment with CCEC of different dose

The tissue histopathology had been shown above after therapy with extraction of *C. colocynthis*. Kidney toxicity is major problem with these types of extracts. The different parts of kidney like glomerulus, thick ascending and descending loops of henle, proximal convoluted tubules and distal convoluted tubules physiology and pathophysiology study.

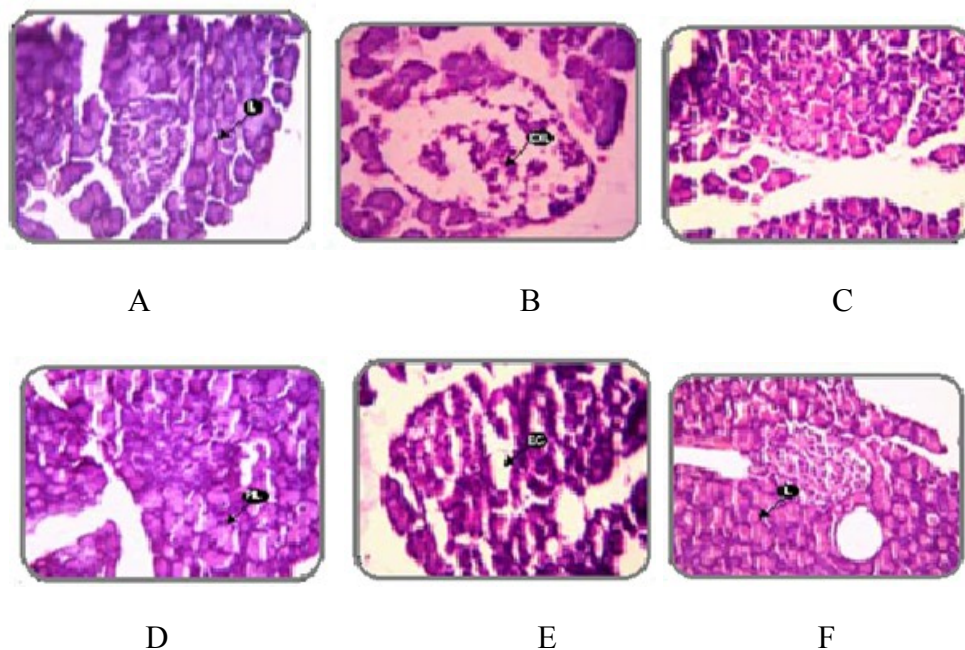


Fig: 7-Histopathology of Pancreas in alloxan induced diabetic animal after treatment with CCEC of different dose

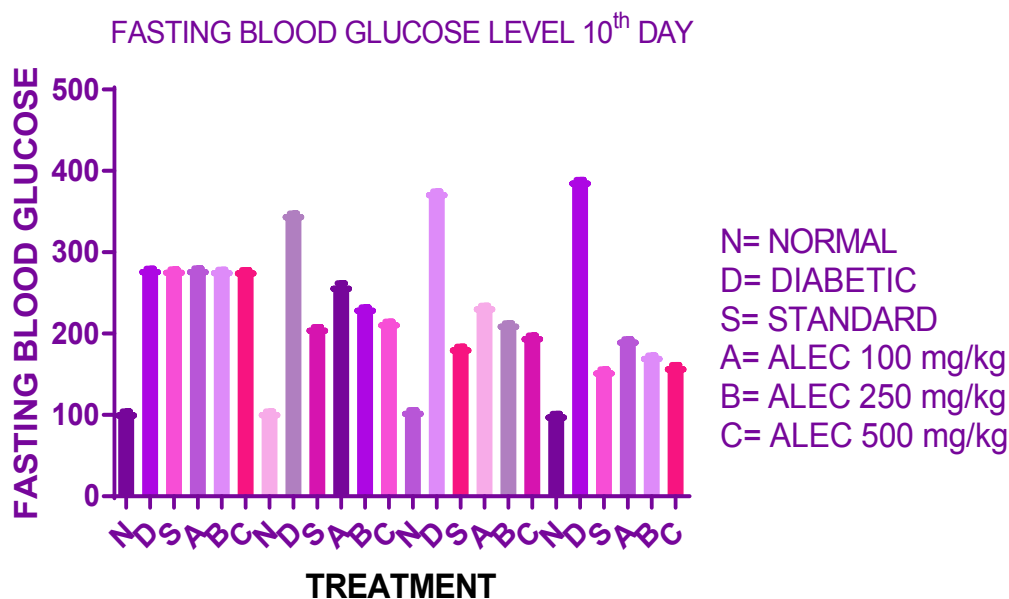
Histopathological Changes of Pancreas Of all treated creature gatherings and controls bunches are inspected Control Rats. A. Gathering I - Pancreas demonstrating exocrine skin break out and endocrine islets (IL); B. Gathering II - Shows drained islets (DIL); C. Gathering III - Shows exocrine skin break out and little saved islets; D. Gathering IV - Shows saved islets (PIL); E. Gathering V-Preserved islets and exocrine (EC) are seen; F. Gathering VI - Pancreas demonstrating islets (IL)

Streptozotocin Induced Diabetic Rat Model

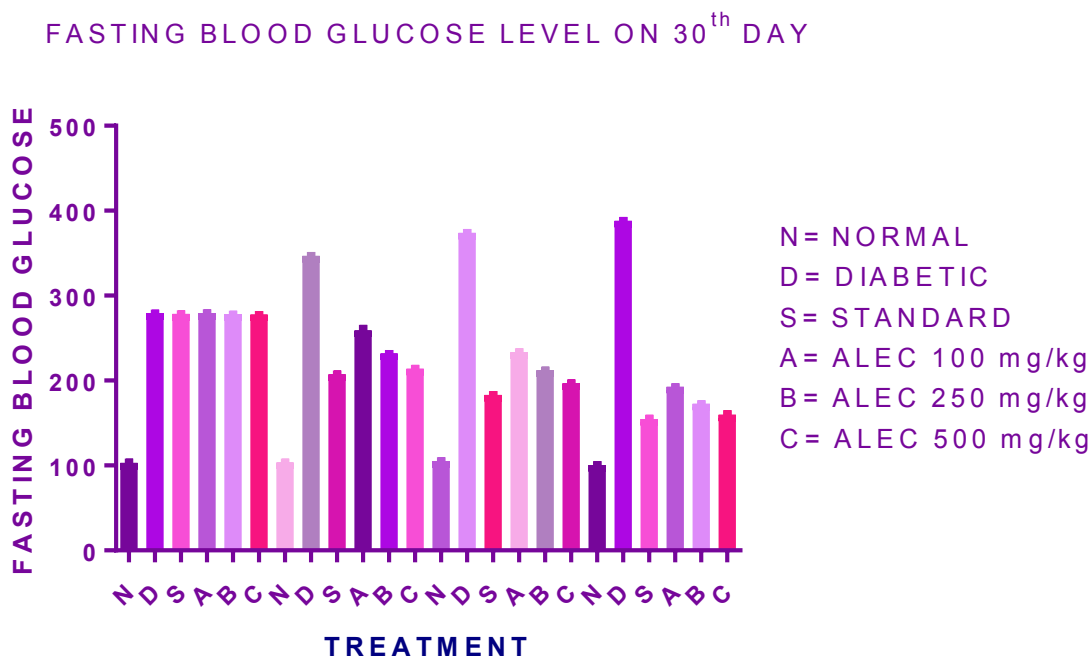
Hostile to diabetic movement of fluid leaves concentrate of *C. colocynthis* (CCEC) in rodents where Being more specifically dangerous to beta-cell than alloxan STZ was utilized for enlistment of diabetes mellitus in test creatures. STZ was utilized as portion of 50.00 mg/kg in intra peritoneal portion as diabetogenic specialist to acquainted diabetic with test rodents. Streptozotocin is offered orally to make creature diabetes.

In intense streptozotocin prompted models fasting blood glucose level was recorded on multi day as basal worth 4.00th 7.00th and 10.00th day. Fluid leaves concentrate of *C. colocynthis* at portion 250.00 and 500.00 mg/kg showed portion subordinate critical enemy of hyperglycemic action on 4.00th 7.00th and 10.00th day post treatment. CCEC portion of 100.00 mg/kg likewise caused decrease in blood glucose level however outcomes were found factually non noteworthy. counter hyperglycemic impact of fluid leaves concentrate of *C. colocynthis* at portion 100.00 mg/kg was discovered less viable than reference standard medications glibenclamide. most extreme decrease was seen on 10.00th day of greatest portion of 500.00 mg/kg CCEC. Glibenclamide produce criticalness decrease in blood glucose level contrast with diabetic control. Glibenclamide teated gathering anyway demonstrated critical decrease in mean fasting glucose at all time focuses. Destining blood glucose level of all rodents treated with *C. colocynthis* came back to basal

level on 10.00th day. Rodents treated with glibenclamide as standard oral hypoglycemic medication stayed underneath basal level on 10.00th day.



Graph: 4- Effect of CCEC on Fasting blood glucose level in STZ induced acute diabetic rat model



Graph: 5- Effect of CCEC on Fasting blood glucose level in STZ induced sub acute diabetic rat model
 In sub intense streptozotocin incited diabetic rodents models fasting blood glucose level was recorded on multi day 14.00th 21.00th and 30.00th day. stamped ascend in fasting blood glucose level saw in diabetic control contrast with typical control rodent. Watery leaves concentrate of *C. colocynthis* at portion 250.00 and 500.00 mg/kg displayed portion subordinate critical enemy of hyperglycemic action on 14.00th 21.00th and 30.00th day post treatment. most extreme decrease os blood glucose was seen on 30.00th day of

greatest portion of 500.00 mg/kg. Glibenclamide treated gathering anyway demonstrated critical decrease in mean fasting glucose at all time focuses. Destining blood glucose level of all rodents treated with *C. colocynthis* came back to basal level on 30.00th day. Rodents treated with glibenclamide as standard oral hypoglycemic medication stayed beneath basal level on 30.00th day.

Impact of watery leaves concentrate of *C. colocynthis* on body weight in diabetes rodent in streptozotocin incited rodent model. Typical control creature were seen as steady in their body weight yet diabetic rodents demonstrated huge decrease in body weight during 10.00 long stretches of treatment with CCEC. Streptozotocin intervened body weight decrease was critical turned around by watery leave concentrate of *C. colocynthis* in portion subordinate design. Impact of test remove at portion 100.00 mg/kg on body weight of creature was found measurably not noteworthy. However, at portion of 500.00 mg/kg was found to factually critical with contrast with diabetic control.

Impact of watery leaves concentrate of *C. colocynthis* on body weight in diabetes rodent in streptozotocin initiated rodent model. Typical control creature were seen as steady in their body weight however diabetic rodents indicated huge decrease in body weight during 30.00 long stretches of treatment with CCEC. Streptozotocin intervened body weight decrease was huge turned around by fluid leave concentrate of *C. colocynthis* in portion subordinate design. Impact of test separate at portion 100.00 mg/kg on body weight of creature was found factually not huge. Be that as it may, at portion of 500.00 mg/kg was found to factually critical with contrast with diabetic control.

Post treatment with CCEC for time of 10.00 days in treatment bunches watched decreased in Serum urea, serum creatinine and serum cholesterol levels when contrast with diabetic control, while serum protein level was expanded essentially when contrast with diabetic gathering. Anyway CCEC portion 100.00 mg/kg neglected to turn around adjusted biochemical parameters. Be that as it may, 250.00 mg/kg and 500.00 mg/kg watched portion depend decrease was found in lipid parameters contrast and diabetic control.

In intense diabetic rodents model which are initiated by streptozotocin. Biochemical parameters are assessed on 10.00th day post treatment with CCEC at portion of 100.00, 250.00 and 500.00 mg/kg. on 10.00th day serum urea was recorded in ordinary benchmark groups as 45.34±02.16 mg/dl diabetic control 93.54±01.87 mg/dl and standard medications treatment bunches was 39.34±01.03 mg/dl and CCEC treatment bunches were 89.84±03.66 mg/dl, 52.34±01.75 mg/dl and 41.17±2.09 mg/dl for 100.00, 250.00 and 500.00 mg/kg separately. From this information we saw in diabetic benchmark groups serum urea was more which are turned around by CCEC. In CCEC treatment bunches most extreme decrease was seen in 500.00 mg/kg followed by 250.00 mg/kg. 100.00 mg/kg likewise decreased serum urea yet it was not hugeness. While glibenclimide utilized as standard.

CCEC at portion of 100.00, 250.00 and 500.00 mg/kg, On 10.00th day post treatment in diabetic creature model which was beforehand diabetes was actuated with streptozotocin. Serum cholesterol levels of all gatherings are recorded. serum cholesterol levels were typical benchmark groups was 74.00±01.78 mg/dl diabetic control 142.5±01.87 mg/dl and standard medications treatment bunches was 86.18±02.31 mg/dl and CCEC treatment bunches were 138.20±04.33 mg/dl, 107.70±01.38 mg/dl and 91.50±01.64 mg/dl for 100.00, 250.00 and 500.00 mg/kg separately. From this information we watched checked expanded in serum cholesterol level in diabetic control contrast with ordinary control rodent. aqueous concentrate of *C. colocynthis* at portion 250.00 and 500.00 mg/kg showed portion subordinate huge decrease was watched. CCEC portion of 100.00 mg/kg additionally caused decrease in serum cholesterol level yet outcomes were found measurably non noteworthy. Fluid leaves concentrate of *C. colocynthis* at portion 100.00 mg/kg was discovered less compelling than reference standard medications glibenclamide.

In intense treatment bunches biochemical parameters are assessed on 10.00th day post treatment with CCEC at portion of 100.00, 250.00 and 500.00 mg/kg which are preceding initiated diabetes with

streptozotocin at portion of 50.00 mg/kg. on 10.00th day serum protein was recorded in ordinary benchmark groups as 05.66±00.81 mg/dl diabetic control 02.66±00.81 mg/dl and standard medications treatment bunches was 04.33±01.66 mg/dl and CCEC treatment bunches were 03.66±01.66 mg/dl, 04.01±01.33 and 04.33±01.63 mg/dl for 100.00, 250.00 and 500.00 mg/kg individually. From this information we saw in diabetic benchmark groups serum protein was less contrast with control, which were turned around by CCEC. In CCEC treatment bunches most extreme recover was seen in 500.00 mg/kg followed by 250.00 mg/kg. 100.00 mg/kg additionally recover serum protein yet it was not essentialness. While glibenclimide utilized as standard medications.

In intense treatment bunches biochemical parameters are assessed on 10.00th day post treatment with CCEC at portion of 100.00, 250.00 and 500.00 mg/kg in streptozotocin incited diabetic rodent's model. on tenth day serum creatinine was recorded in ordinary benchmark groups 00.97±00.01 mg/dl diabetic control 01.08±00.12 mg/dl and standard medications treatment bunches was 00.63±00.10 mg/dl and CCEC treatment bunches were 00.92±00.55 mg/dl, 00.71±00.01 and 00.61±00.003 mg/dl for 100.00, 250.00 and 500.00 mg/kg separately. From this information we watched stamped expanded in serum creatinine level in diabetic control contrast with ordinary control rodent. Watery leaves concentrate of *C. colocynthis* at portion 250.00 and 500.00 mg/kg displayed portion subordinate critical decrease was watched. CCEC portion of 100.00 mg/kg likewise caused decrease in serum creatinine level however outcomes were found factually non huge. Watery leaves concentrate of *C. colocynthis* at portion 100.00 mg/kg was discovered less compelling than reference standard medications glibenclamide.

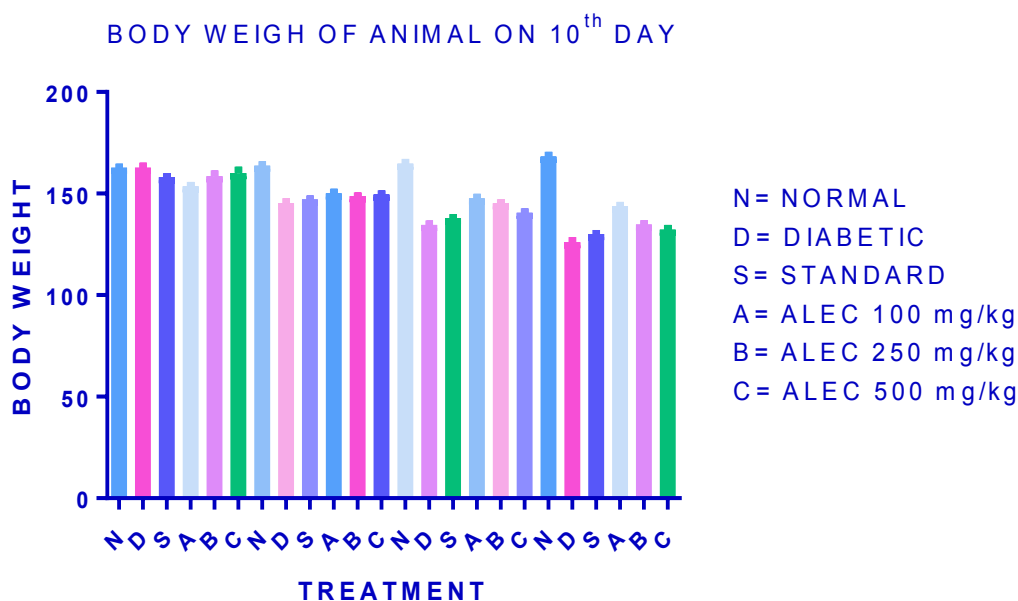
In sub intense treatment bunches biochemical parameters are assessed on 30.00th day post treatment with CCEC at portion of 100.00, 250.00 and 500.00 mg/kg in streptozotocin incited diabetic rodent's model. on 30.00th day serum creatinine was recorded in typical benchmark groups 00.97±00.01 mg/dl diabetic control 01.10±00.10 mg/dl and standard medications treatment bunches was 00.60±00.10 mg/dl and CCEC treatment bunches were 00.97±00.01 mg/dl, 00.71±00.03 and 0.58±0.07 mg/dl for 100.00, 250.00 and 500.00 mg/kg separately. From this information we watched stamped expanded in serum creatinine level in diabetic control contrast with typical control rodent. Watery leaves concentrate of *C. colocynthis* at portion 250.00 and 500.00 mg/kg displayed portion subordinate huge decrease was watched. CCEC portion of 100.00 mg/kg likewise caused decrease in serum creatinine level however outcomes were found factually non huge. reference standard medications glibenclamide was utilized.

In sub intense diabetic rodents model which are initiated by streptozotocin. Biochemical parameters are assessed on 30.00th day post treatment with CCEC at portion of 100.00, 250.00 and 500.00 mg/kg. on 30.00th day serum urea was recorded in typical benchmark groups as 46.82±01.47 mg/dl diabetic control 90.07±01.04 mg/dl and standard medications treatment bunches was 39.00±01.41 mg/dl and CCEC treatment bunches were 87.50±01.25 mg/dl, 53.00±01.41 mg/dl and 37.00±03.50 mg/dl for 100.00, 250.00 and 500.00 mg/kg separately. From this information we saw in diabetic benchmark groups serum urea was more which are switched by CCEC. In CCEC treatment bunches most extreme decrease was seen in 500.00 mg/kg followed by 250.00 mg/kg. 100.00 mg/kg likewise diminished serum urea however it was not centrality. While glibenclimide utilized as standard.

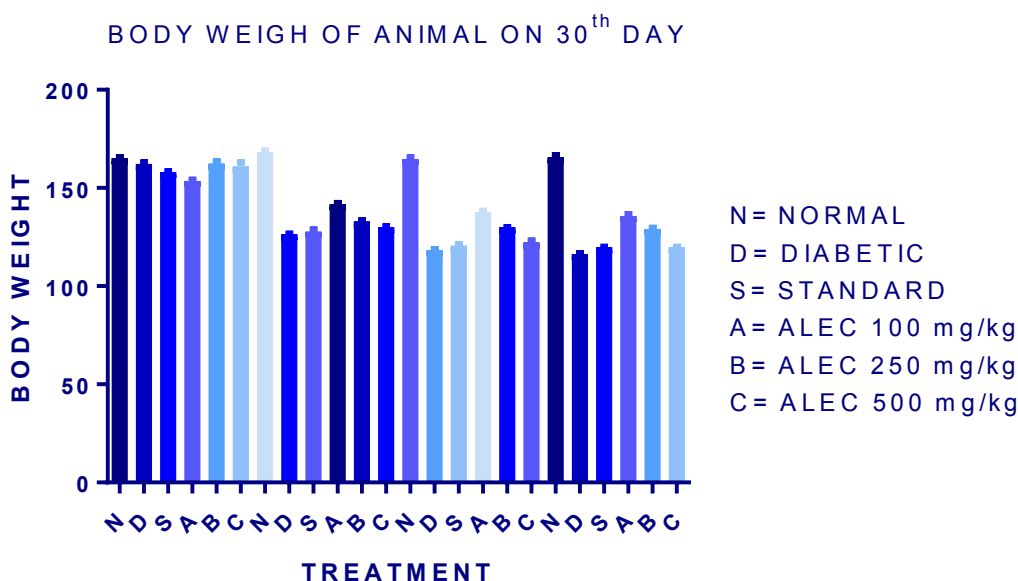
CCEC at portion of 100.00, 250.00 and 500.00 mg/kg, On 30.00th day post treatment in diabetic creature model which was already diabetes was instigated with streptozotocin. Serum cholesterol levels of all gatherings are recorded. serum cholesterol levels were typical benchmark groups was 74.00±02.00 mg/dl diabetic control 140.70±01.63 mg/dl and standard medications treatment bunches was 81.69±01.63 mg/dl and CCEC treatment bunches were 136.50±01.25 mg/dl, 114.50±01.42 mg/dl and 86.00±00.89 mg/dl for 100.00, 250.00 and 500.00 mg/kg individually. From this information we watched stamped expanded in serum cholesterol level in diabetic control contrast with ordinary control rodent. Fluid leaves concentrate of

C. colocynthis at portion 250.00 and 500.00 mg/kg displayed portion subordinate critical decrease was watched. With reference standard medications glibenclamide.

In sub intense treatment bunches biochemical parameters are assessed on 30th day post treatment with CCEC at portion of 100.00, 250.00 and 500.00 mg/kg which are preceding actuated diabetes with streptozotocin at portion of 50.00 mg/kg. on tenth day serum protein was recorded in ordinary benchmark groups as 05.66±00.81 mg/dl diabetic control 03.11±00.40 mg/dl and standard medications treatment bunches was 04.83±00.75 mg/dl and CCEC treatment bunches were 03.16±01.05 mg/dl, 03.15±00.80 and 04.66±00.51 mg/dl for 100.00, 250.00 and 500.00 mg/kg separately. From this information we saw in diabetic benchmark groups serum protein was less contrast with control, which were turned around by CCEC. In CCEC treatment bunches greatest recapture was seen in 500.00 mg/kg followed by 250.00 mg/kg. 100.00 mg/kg additionally recover serum protein however it was not centrality. While glibenclimide utilized as standard medications.



Graph: 6- Effect of CCEC on body weight in STZ induced acute diabetic rat model



Graph: 7- Effect of CCEC on body weight in STZ induced sub acute diabetic rat model

HISTOPATHOLOGICAL STUDY

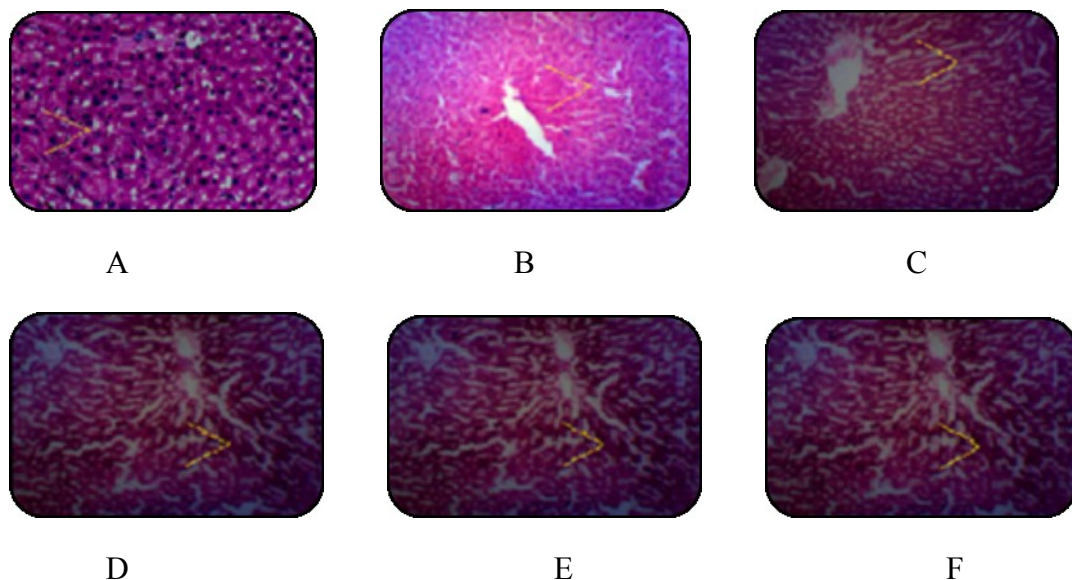


Fig: 8- Histopathology of liver in STZ induced diabetes rat model after treatment with CCEC in different dose.

A- Control liver (Nhp: Normal hepatocytes)

B- Diabetic liver (STZ treated) (Dhp: Damaged hepatocytes)

C- Glibenclamide treated liver (Standard Drug)

D, E, F- C. COLOCYNTHIS treated liver (Rhp: Recovered hepatocytes)

Histopathology of Pancreas

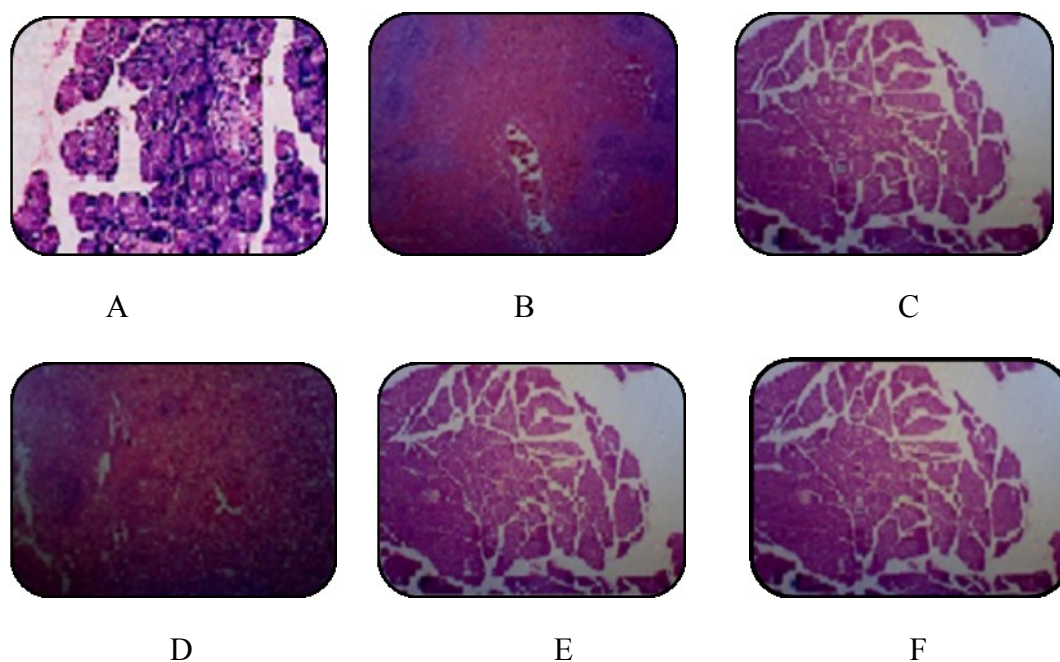


Fig: 9- Histopathology of Pancreas in STZ induced diabetes rat model after treatment with CCEC in different dose.

Histopathology of Kidney

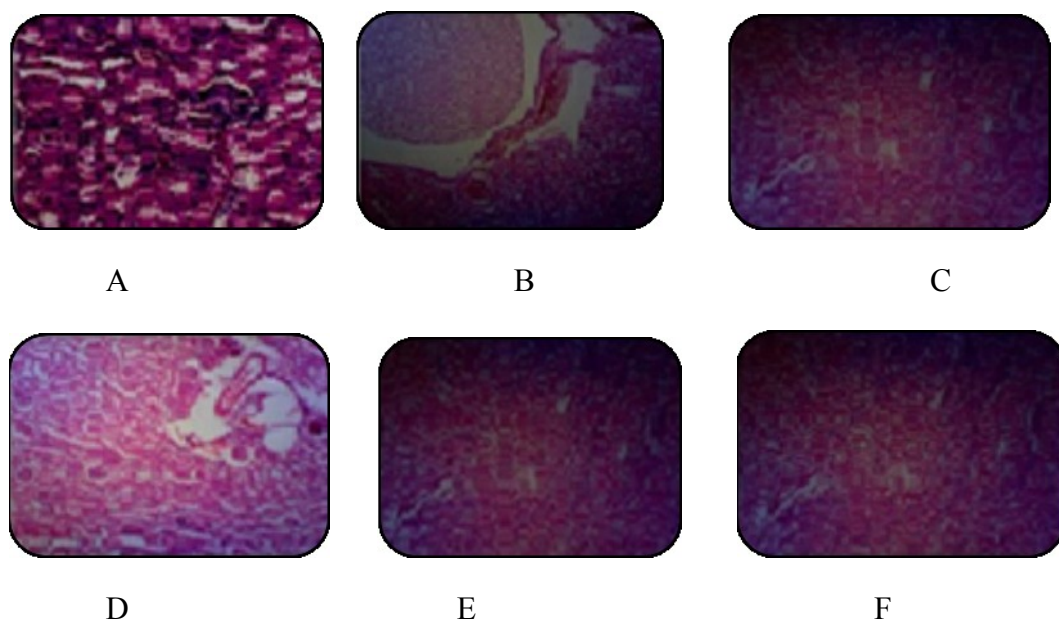


Fig: 10- Histopathology of Kidney in STZ induced diabetes rat model after treatment with CCEC in different dose.

Rat Hemidiaphragm Method

Glucose uptake by isolated rat hemi-diaphragm: Glucose take-up by rodent hemi-stomach was evaluated by techniques depicted somewhere else (Walaas, 1952) with certain adjustments. Estimation of glucose content in rodent hemidiaphragm was utilized for in vitro investigation of fringe take-up of glucose. Qualities are introduced in table.

For glycogen content

The hemi stomachs were brooded in tyrode arrangement with glucose (2.00%) in comparable path concerning glucose take-up. Just time will be reached out to hour and half. Following brooding hemi stomachs will be flushed for 10.00-15.00 sec in 0.90% NaCl at 0°C to wash off outside glucose and to stop catalyst action. It will be smudged, solidified on dry ice and glycogen substance of tissue will be estimated by anthrone technique for carroll et al. glycogen substance will be communicated in microgram/milligram of tissue of rodents hemidiaphragm.

CONCLUSION

Alloxan (120.00 mg/kg b.w) was found to initiate diabetes in rodents as prove by expanded glucose levelling in blood.

a. Intense Alloxan instigated DM (10.00 days treatment)

In intense alloxan instigated diabetic models Revealed portion subordinate antidiabetic potential in rodents with dosages of 100.00, 250.00 and 500.00 mg/kg b.w. portion of 500.00 mg/kg b.w/day was seen as having greatest activity, and impact was seen equivalent to levels of blood glucose with standard antidiabetic tranquilize, glibenclamide.

- Exhibited fundamentally hypoglycemic impact in rodents.

- Non-huge increment in kidney work tests, i.e., serum urea levels, serum creatinine levels and serum absolute protein levels.

- Significantly turned around decline in wt. of body found in diabetes.

- Glibenclamide, utilized as standard antidiabetics tranquilize was seen as progressively viable as it essentially diminished blood glucose levels while it had non critical impact on different parameters.

b. Sub Acute Alloxan actuated Diabetes mellitus (30.00 days treatment)

In sub intense alloxan actuated diabetic models Revealed portion subordinate antidiabetic potential in rodents with dosages of 100.00, 250.00 and 500.00 mg/kg b.w. portion of 500.00 mg/kg b.w/day was seen as having greatest activity, and impact was seen equivalent to levels of blood glucose with standard antidiabetic medicate, glibenclamide.

Exhibited fundamentally hypoglycemic impact in rodents.

on-huge increment in kidney work tests, i.e., serum urea levels, serum creatinine levels and serum all out protein levels.

Significantly turned around decline in body weight found in diabetes.

Glibenclamide, utilized as standard antidiabetic tranquilizes was seen as progressively powerful as it essentially diminished blood glucose levels while it had non huge impact on different parameters.

Looking at both outcomes we presume that greatest impact was found in sub intense treatment bunches at portion 500.00 mg/kg.

c. Histopathology

watery leaves concentrate of *C. colocynthis* when regulated (100.00, 250.00 and 500.00 mg/kg b.w) to rodents demonstrated islet structure with hardly any incendiary cells at portion of 100.00 mg/kg b.w while at portion level of 500.00 mg/kg b.w indicated not many fiery cells in islet of pancreas.

- No variation from norm in livers
- No variation from norm in kidneys.

No variation from norm in pancreas

Streptozotocin (50.00 mg/kg b.w) was found to initiate diabetes in rodents as prove by expanded blood glucose levels.

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How to cite this article: Kamal, and Rakesh Kr. Jat. "EVALUATION OF ANTIDIABETIC ACTIVITY OF ETHANOLIC EXTRACT OF CITRULLUS COLOCYNTHIS". *Tropical Journal of Pharmaceutical and Life Sciences*, vol. 9, no. 3, June 2022, pp. 16-38, <https://informativejournals.com/journal/index.php/tjpls/article/view/1>

PUBLISHED BY:
INFORMATIVE JOURNALS
JADOUN SCIENCE PUBLISHING GROUP INDIA

