

SCREENING OF ANTIDIABETIC ACTIVITY OF DILLENIA INDICA ROOT EXTRACT

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ABSTRACT

The current review was done to explore the antidiabetic and hypolipidemic exercises of bioactive portion (ethyl acetic acid derivation part) of Dillenia indica, which has promising impacts in treating diabetes and other diabetic-related complexities. Despite its wide use in the Northeast locale of India as conventional medication, there is just a single clinical review where the antidiabetic capability of the natural product powder has been shown. The blood glucose level was assessed at week after week spans by glucometer. Serum cholesterol, fatty substances and high-thickness lipoprotein cholesterol (HDL-C) were likewise assessed in ordinary and diabetic rodents by an autoanalyzer. D. indica have antidiabetic property too further develop body weight, liver profile, renal profile and absolute lipid levels. DIME has likewise positive impact to repress the histopathological changes of the pancreas and kidney in alloxan actuated diabetes. D. indica showed huge hindrance of AGEs arrangement in vitro. D. indica created huge weakening in the glycaemic status, renal boundary, lipid profile and level of cancer prevention agent chemicals demonstrating viability in diabetic nephropathy. Additionally, D. indica created critical decrease in the development of AGEs in kidneys. The current review reasons that D. indica as a potential remedial specialist against diabetic nephropathy.

Keywords: *Dillenia indica, Advanced glycation end products; Botulinic acid; Hyperglycaemia; Oxidative stress.*

INTRODUCTION:

India is called as a professional flowerbed of the entire world because of the biggest maker of restorative plant and spices. Diabetes is the most widely recognized non-infectious illness universally. In a review assessed number in 2007 of grown-ups with diabetes was 246 million. 80% are live in non-industrial nations. The biggest situation on the Indian body of land and China^[1]. According to this 85-95% cases are type 2 diabetes and, in the world, this is a major disorder of the people health and that at least until 2025 there will be about 380 million adults. Now there are 41 million patients in India and it will be increased 70 million in future(2025). As per the WHO estimation the developing townships regions it will be increasing to 3.9 billion in 2030 as of now ranging from 1.9 billion in 2000^[2]. WHO listed more than 21000 medicinal plants are used traditionally in a large scale. There is an enormous

growth in the medicinal and herbal industry from the last few years. There many medicinal formulations popular in the developed as well as the developing countries [3]. They are traditionally used from 1000 years ago. Herbal medicines a natural origin and they have less side effect on human beings and environment. Many synthetic drugs are derived from the medicinal plant.

DIABETIES:

The term diabetic mellitus is related to the chronic insulin resistance disorder of various etiological specification with chronic increase in the glucose level (hyperglycemia) by dis-balance of carbohydrate, protein, fat metabolism. They are creating the disturbance in insulin action, insulin secretion.

Diabetes mellitus (DM) is the group of different type of diseases; like cardiovascular problems, coronary artery disease with angina (chest pain), heart attack, stroke as it cause restriction in arteries , the longer duration of diabetes have the higher chances to develop heart disease (**Ramachandran et. all**). Diabetes is a major health problem in India. Diabetes is leading losses of economic life. Diabetes is a chronic disorder which cause due to the imbalance in insulin level in blood. These are abnormal increase blood sugar level. Herbs and botanical ingredient are very beneficial effect show on maintain blood sugar levels in pre-diabetic and post diabetic. [4]

TYPES OF DIABETES AND OTHER CATEGORIES OF GLUCOSE REGULATION: (Dr.RashaSalama)

1. Type 1 diabetes (beta -cell destruction, usually leading to absolute insulin deficiency)

- a) Immune -mediated diabetes.
- b) Idiopathic diabetes.

2) Type 2 diabetes (ranging from predominantly insulin resistance with relative insulin deficiency to predominantly an insulin secretory defect with insulin resistance).

3) Other specific types of diabetes:

- a) Genetic defects of the beta cell.
- b) Genetic defects in insulin action.
- c) Diseases of the exocrine pancreas.
- d) Endocrinopathies.
- e) Drug or chemical – induced diabetes.

SIGN AND SYMPTOMS: There are few sign and symptoms of Type 1 diabetes mellitus as Polyuria, Increased thirst, Irritability, Skin dryness and extreme hunger whereas Polydipsia, Patients can be asymptomatic, Polyuria, Feeling tired. And Slow healing of cut and wound are symptoms of Type 2 diabetes mellitus

TABLE: CAUSE OF DIABETES:

S.no.	Diabetes	Cause
1	Type 1	It to be an autoimmune condition. That's means your immune system by mistakenly attack and kill the beta cell in your pancreas which produce insulin which is responsible for the diabetes. They destroy it permanently. These are genetic and environmental both reasons. Lifestyle are not a reason to cause of diabetes.
2	Type 2	It starts as insulin resistance. Its mean your body can not use insulin systemically. Which stimulate pancreas resulting in production of increased insulin until demand is fulfilled and the production of decreased, which conduct to the high blood glucose.
3	Gestational	During pregnancy there are hormones that blocks insulin are produced. This type occurs only during pregnancy.

FACTORS EFFECTING DIABETES:

- 1) Genetics.
- 2) Environment.
- 3) Viruses.
- 4) Diet.
- 5) Stress.
- 6) Immunological.
- 7) Malnutrition inutero.
- 8) Age.
- 9) Pregnancy.
- 10) Insulinresistance.
- 11) Pancreatic beta cell failure.

TREATMENT:

There are several anti-diabetic medications are created to settle and control blood glucose levels among individuals with diabetes. Hostile to diabetic medications is normally used to oversee diabetes.^[5] Various types of Anti-diabetic drugs are there that includes; Insulin., Pramlintide (Amylin), GLP-1 receptor against (Byetta& Victoza) and Oral Hypoglycemic (Tablets).

Table: Synthetic Drug Used For the Treatment Of Diabetes

S.no.	Drug	MOA	Side Effects
1	Glimepiride, Glipizide, Glyburide	Closing of ATP Sensitive potassium-channels present in the beta Cells of the plasma membrane	Low blood glucose levels, Itching, Upset stomach, Weight gain
2	Biguanides (Metformin)	Decrease hepatic glucose production, Decrease inertial Absorption	Sickness with Alcohol, Kidney Complication, Metal Taste, Tiredness as

			dizziness
3	Acarbose, Maglitol	By competitive and reversible inhibition of intestinal alpha-Glycosidase, Delays carbohydrates digestion, reduce rate of glucose absorption.	Gas, Bloating and Diarrhea
4	Pioglitazone, Rosiglitazone	Improve metabolic control through improvement of insulin sensitivity, reduce insulin resistance in adipose tissue, Muscle & Liver	Gaining of weight, risk of anemia and liver diseases, Inflammation of Ankles and Lungs.
5	Meglitinides	Results in Insulin release and Calcium influx by opening the Voltage gated Calcium channels	Low Blood Sugar, Weight Gain.

Limitations of Modern Medication

Group	Limitation
Sulfonylureas	Long duration of action & Higher risk of hypoglycemia, Variation in duration of action Between Individuals
Metformin	Lactic acidosis in patients with high risk of hypoxia, hyper fusion, renal insufficiency limit its usage for in patient management
Thiazolidinediones	Slow onset of action & contraindication in heart failure makes them unsuitable for in patient management

Due to the lethal side effect and Contraindications of Synthetic Drugs like Pregnancy, lactation, Renal and hepatic impairment, Heart failure, Part history of lactic acidosis, Chronic lung disease, All other situations where OHGAs is contraindicated. In such case use of Herbal Drug is Necessary which have less side effect. There are several herbs like Fenugreek, Turmeric, Garlic, Neem, Onion, Cinnamon, Coconut, Babul which have potent chemical compounds like Flavonoids, Vitamine, Saponins, Cysteine, Glutathione, Alkaloids, Tannins, Sulphur Compounds which are popularly used as antidiabetic agent ^[6,7].

Discription of Plant

Dillenia indica

Family: Dilleniaceae

Species: Indica Linnaeus

Synonyms: Elephant Apple

Biological source: It obtain from the dried roots of the plant of **Dillenia Indica**

Parts used: Aerial parts, Root

Other species: *Dillenia Elliplica Thumb*, *Dillenia elongate miq*, *Dillenia speciosa Thumb*, *Dillenia Indica*

Habitat: EvergreenForest or tropical rain forest, along river

Temperature: They best growth in regions where yearly daytime temperatures are inside the scope of 30-40°C however can endure 7.47°C.

Propagation: Propagated by seed, semi-ripe cutting.

Altitude: The teak forest in Javathe altitude is about 1100 meters. Soil range: Prefer a good sunny position in loamy sand that is well drained. Grows best in a rich slightly acid soil

Rainfall: It prefer a yearly rainfall in between 3,000-4,000mm but the maximum should be 2,000-5,500 mm.

PH: Prefer in the range of 5.5-7, tolerate in 8 pH.

Fertilizer: Apply any organic fertilizer.

Botanical Description:

It is an evergreen plant with enormous bush. The height varies nearly 6-15 meter with spread branches and thick bark. Blossom time is March - May and simple to develop. The flowers are large in size, flower petals are white in colour, 15-20cm diameter and numerous yellow stem, sepals 2cm broad 4cm long and concave and orbicular. Large fruit size and the colour of fruit is greenish yellow orange, mucilaginous, 5-12cm across. The level of trunk is about 30-80 feet and the circumference is 6ft with the thick adjusted crown. Roots are yellowish brown in colour, rounded in shape, fibrous. Petals are oblong in shape. Leaves are 15-36cm long with conspicuously corrugated surface. Seeds are small, dark brown in colour. (Md.H.abdille Jena2 Sep 2004)

Geographical distribution: *Dillenia Indica* found in the tracts of Himalaya, from Kumaon & Garhwal, Bengal and Assam, Southern India, South words to central, also in Myanmar, Malaysia, Thailand, Bangladesh, Sri Lanka and Nepal. (2013 Dipal Gandhi & Priti Mehta)

Chemical Constituents: Sepals contain Tannin, glucose, malic acid. The bark & leaves are contained tannins, cyclooctenone, n-hentriacontane, Botulinic acid & beta sitosterol. Fruits contain polysaccharide arabinogalactan. (From Paryayurveda.com) Glycoside, Steroids, flavonoids & saponins, reducing sugar, trihydroxy-3, dimethyl flavone, stigmaterol, Betulinaldehyde, lupeol, myricetin hydroxy-lactone, dihydro-isorhamnetin, myricetin, hydroxylactone. (Apurba Talukdar 2012)

Pharmacological Uses based on scientific evidence:^[8,9]

Antioxidant: Fruit of *Dillenia indica* has been investigated. In methanol, petroleum ether and water extracts of shade dried fruits. Their ethyl acetic acid derivation concentrate of stem bark of *Dillenia indica* shows in-vivo calming and pain relieving expected in trial creatures. Anti-diarrheal activity investigated from the bark of *Dillenia indica* in methanolic extract. These movement concentrated by utilizing magnesium sulphate and castor oil actuated diarrheal model and charcoal prompted gastro intestinal motility in mice. Stem ethanolic & oil ether concentrate of *Dillenia indica* stem barks showed cytotoxic impacts bark with methanolic separate (Chandan Choudhury Baruo et al 2018). Petroleum ether extract of *Dillenia indica* is highly against antimicrobial properties against gram positive or gram-negative bacteria. Methanolic extract are lowering potential after oral administration (Latifhaisaifulyan & Nurdin Armania 2014). **Hypoglycemic effect:** The fruit powder of

Dillenia indica shows highly significant result to reducing the FBS & PPBS level. Mending impact: *Dillenia indica* natural product separates prompted psoriasis like injuries in wistar rats. Analgesic, CNS depressant: There methanolic extract shows neurons pharmacological, analgesic and cytotoxic effect.

Traditional (Ethno botanical) Uses:^[10]

It is additionally utilized customarily in different pieces of north-east India, the juice of leaves; bark savoured the therapy of disease and looseness of the bowels. In India *Dillenia indica* fruit juice is used to prepare various dishes & desserts. It mashes of the organic product is blend in with water to clean the scalp hair. By its new Juice of Bhavya organic product serves to worked on stomach related limit and absence of appetite. Decoction of the bark is utilized in oral thrush and to eliminate terrible request from mouth. Its juice is cold infusion is a good hair tonic and help to regenerate in hair fall. It's used in the treatment of cough & dyspnoea with the mixture of honey & sugar with freshly prepare fruit juice. (Barva et al 2018) some Contraindications are Renal & hepatic impairment, heart failure.

Material and Methods

- The Plant material is required for the preparation of a hydro alcohol extract included the fresh roots of *Dillenia Indica* were collected from neighbourhood herbal garden in Dehradun in the month of August and authenticated by Department of Botany, FRI, Dehradun.

Preparation of Ethanolic Extract for activity

The roots were taken out. The roots material was cleaned and dried in shade and after drying the drug grinded into powdered structure. The medication was stuffed into an impenetrable compartment. The grinded substances were sieved by 18 mesh size sieves in order to ensure uniform size. For the preparation of aqueous and alcohol extract of plant powder is subjected to cold maceration. For this process 250 gm plant powder was dipped into 500 ml petroleum ether for 48 hours for defattification and after plant material completely soaked. Solvent is removed by filtering it through muslin cloth & liquid extract was evaporated by keeping extract in china dish and kept them on water bath. After this the previous extractable plant material again spreaded over the filter paper for 15 minutes and after that again soaked into 500 ml eaker containing 500 ml alcohol and water in ratio of 70:30 and kept it for 48 hours. After completion of time duration solvent is again removed by filtering it through muslin cloth & liquid extract was evaporated on water bath^[11].

Quantitative Investigation of Plant Material:^[12]

Extractive value: These are valuable for assessment of unrefined medications and given a thought regarding the idea of synthetic are available in them. How much extractive a medication respect a given dissolvable is after an inexact proportion of a specific constituent or gathering of related constituent the drug contains.

Ash Value: The complete debris is the buildup staying after burning. The corrosive insoluble debris is the piece of the absolute debris which is insoluble in weakened HCL. Debris esteem are useful to decide the quality and virtue of the rough medications in powder structure.

Ash Value: The absolute debris is the buildup staying after burning. The corrosive insoluble debris is the piece of the all-out debris which is insoluble in weakened HCL. Debris esteem are useful to decide the quality and virtue of the unrefined medications in powder structure. Assurance of complete debris:

$$\text{Ash value} = (\text{Initial wt.} - \text{Final wt.}) / \text{Initial wt.} \times 100$$

Water soluble ash: To determine the drugs water solubility. Add 25 ml distilled water in total obtain ash & boiled for 5 minutes, filter the solution with watchman filter paper & place the filter paper into crushable than in muffle burner. Finally, wt. and calculation done.

Acid insoluble ash: To determine the drugs acid solubility. Add 25 ml of HCL in total ash obtain & boil for 5 min. Filter the solution by watchman filter paper placed the filter paper in crushable and placed it into muffle burner. Finally, wt. and calculation done.

Chemical Investigation:^[13,14]

Test for AminoAcids

- **Ninhydrin Test (General Test):** 3ml of test arrangement was warmed with 3 drops of 5% Ninhydrin arrangement on bubbling water shower for 10min. Purple colored as showed up.

1. Test for carbohydrates

- **Molisch's Test (General Test):** To 2-3ml of the concentrate was taken and a couple of drops of alpha-naphthol arrangement in 95% liquor was added. Then it was shaken and conc. Hydrochloric corrosive was added from the side of the test tube. A Violet ring was framed at the intersection of two fluids.

2. Test for steroids

Salkowski test: To 2ml of concentrate, added 2ml of chloroform and 2ml of cone. H₂SO₄ and shaken well. Chloroform layer seemed red and corrosive layer showed greenish yellow fluorescence.

3. Test for Proteins

- **Biuret Test (General Test):** 3ml of test arrangement was added to 2ml of 4% NaOH and barely any drops of 1% CuSO₄ arrangement. Violet tone was showed up.

4. Test for Glycosides

- **Killer-killani test:** 2ml concentrate were blended in with 1ml of icy acidic corrosive, one drop of 5% FeCl₃ and conc. H₂SO₄ Reddish earthy colored tone showed up at

intersection of the two fluids layers and upper layer seemed somewhat blue green.

5. Test ofalkaloid

Dissipated the fluid, drunkard and chloroform extricate independently. To buildup, added weaken HCL Shaken well and separated. With filtrate, Perform following tests.

- **Dragondroff's test:** 2-3ml of test arrangement was blended in with 3ml of Dragondroff's official. Orange-brown ppt. was framed.
- **Mayer's test:** 2-3ml of test arrangement was blended in with 3ml of Mayer's reagent. While tone ppt. was framed.
- **Hager's test:** 2-3ml of test arrangement was blended in with 3ml of Hager's reagent. No precipitation wasformed.

6. Test forFlavonoids

- **Shinodatest:** to dry powder or concentrate, added 5ml 95% ethanol, then barely any drop conc. HCl and 0.5gm magnesium turnings. The pink color observed.
- To the little amount of buildup, added lead acetic acid derivation arrangement. Yellow-hued accelerates were formed.
- Expansion of expanding measure of sodium hydroxide to the buildup showed no yellow tinge.

7. Test for tannins and phenolic compounds

- To 2-3ml of watery and alcoholic concentrate, added not many drops of the following reagents.
- 5% FeCl₃ arrangement: dark blue-dark tone.
- Lead Acetate arrangement: White ppt.
- Gelatin arrangement: white ppt.
- Bromine water: De-hue of bromine water.
- Acidic corrosive arrangement: red variety arrangement.
- Weaken Iodine arrangement: transient red tone.
- Weaken HNO₃: ruddy to yellow tone.

Pharmacological activity:

Salivary amylase inhibition method- the salivary amylase assay was performed according to the method described by Odeyemi. (Idowu Jonas Sagbo et al2018)

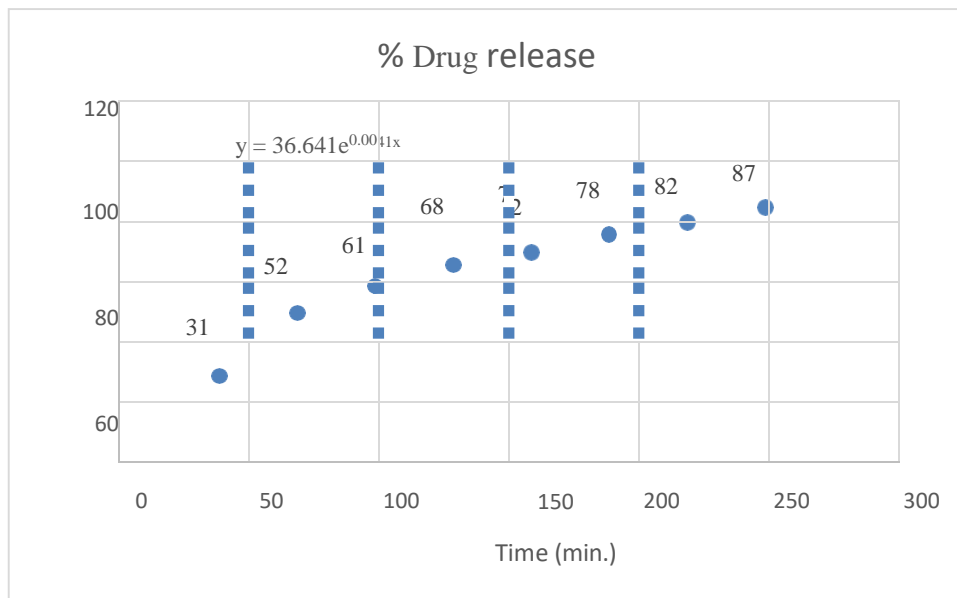
Calculation of 50% inhibitory concentration (IC50): The grouping of the plant separate expected to rummage 50% of the extremists (IC50) was determined by utilizing the searching

exercises at five distinct centralizations of the concentrate % restraint (I%) was determined by (ShaiL.J.2010)

$$I \% = (AC-AS) / AC \times 100$$

Where AC is the absorbance of the control and AS is the absorbance of the example.

% Drug release: Calibrationcurve



RESULTS AND DISCUSSION

Quantitative Investigation Physicalconstants

The level of absolute debris, corrosive insoluble debris, water-solvent debris, and different extractive qualities for Dillenia Indica are recorded in [Table 4. 1].

Table: Pharmacognostic Evaluation of the dried powdered plant parts of *Dillenia Indica* (root).

S.no.	Evaluation Parameters	Value (% w/w) roots
1	Total Ash Value	12.55 ±0.91
2	Water Insoluble Ash Value	7.75 ±0.52
3	Acid Insoluble Ash Value	4.18 ± 0.58
4	Extraction Value	16.15 ±0.33

*Mean value of five counts.

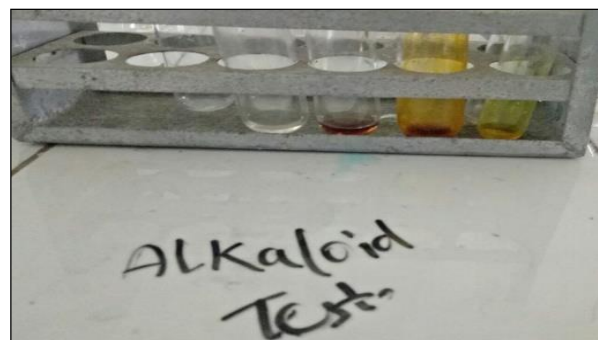
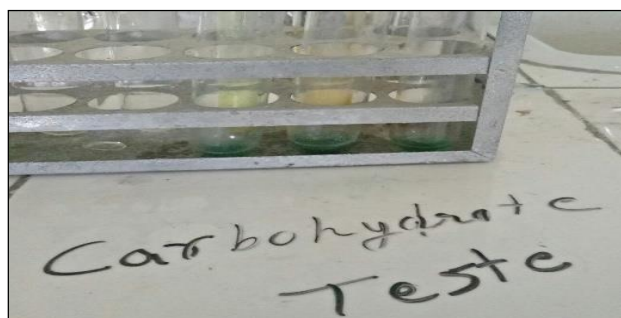
Chemical investigations on different extracts

Phytochemical investigation of *Dillenia Indica* root (Table 4. 2), with the ethanolic extracts were rich in most active constituents like alkaloids, flavonoids and terpenoids.

Table: Phytochemical investigation of *Dillenia Indica* root extracts

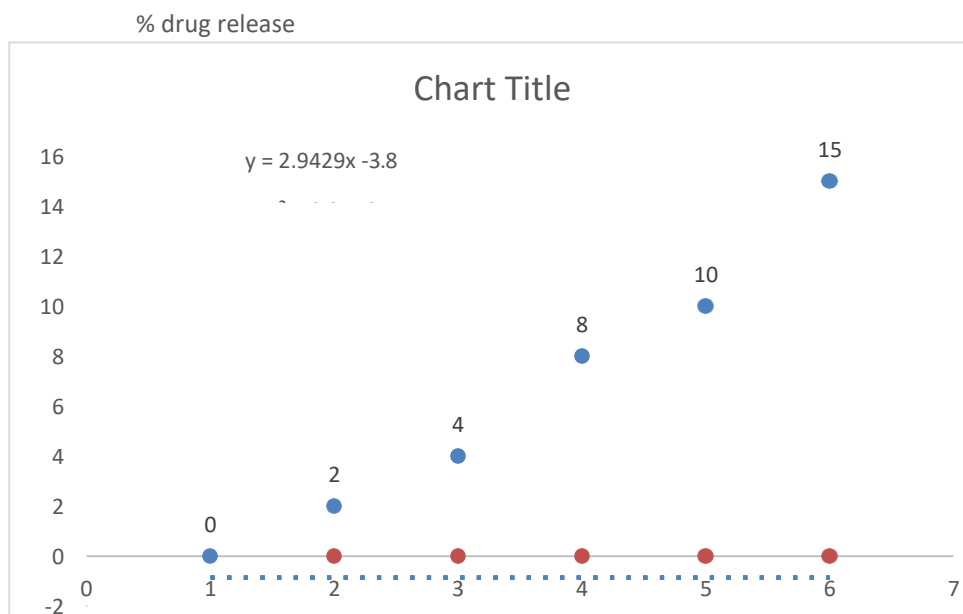
S.No.	Plant Constituents Test/Reagent Used	Ethanolic Extract
1	Test For Carbohydrates	
	Molisch's Test	+
2	Test For Alkaloids	
	Mayer's Test	+
	Wagner's Test	+
	Hager's Test	
3	Test For Glycosides	
	Keller-Killani's Test	+
4	Test For Flavonoids	
	Shinoda's Test	+
5	Test For Tannins And Phenolic Compounds	
	5% FeCl ₃ Solution	+
	Reaction with copper sulphate	+
	Reaction with lead acetate	+
	Reaction with Potassium Dichromate	+
	Drug + K ₃ Fe (CN) ₆ + NH ₃	+
6	Test For Steroid	
	Salkowski Test	+
7	Test For Proteins	
	Biuret Test	--

(+) Identification tests gave positive results.(□) Identification tests gave negative results.



4.4 Pharmacological Evaluation: Absorbance of Ethanolic extract:

S.No.	Plant Extract	Conc. ug/ml	Absorbance	IC50
1	Ethanolic Extract of DilleniaIndica	2	0.011	27.101
		4	0.0108	28.94
		8	0.0107	31.21
		10	0.0109	32.18
		15	0.0108	35.87



Absorbance of standard drug (Acarbose):

S.No.	Standard Drug	Conc. Ug/ml	Absorbance (nm)	% Inhibition
1	Acarbose	2	540	27.14
		4	540	29.01
		8	540	31.25
		10	540	32.52
		15	540	35.91

R= Purity of drug- R is closer than 1 the purity of the drug is more.

Conclusion:

The in vitro studies for salivary amylase inhibitory activity were done for antidiabetic activity evaluation of *Dillenia Indica*. Using crude extract with ethanolic solvent. In this study, the enzyme inhibitory activity of crude extract isolated from roots of *Dillenia Indica* was compared with Acarbose standard drug. The consequence of this study guides further exploration to assess the helpful possibilities of foundations of *Dillenia Indica* in the administration of hyperglycaemia and typr-2 diabetes either alone or in a mix treatment. The present study indicated that *Dillenia Indica* could be very useful in diabetes treatment.

Future Prospects:

Dillenia Indica indicates a prominent and mostly preferred and economic treatment in future. Due to less side effect and diverse chemical composition different dosage formulation can be developed using *Dillenia Indica* as an active pharmaceutical ingredient.

ANNOUNCEMENT OF INTEREST

The creators report no irreconcilable circumstances. The writers are liable for the substance and composing of the paper. Creator profoundly grateful to UIPS, Uttaranchal University, Dehradun for giving the all office to completed my examination work.

IRRECONCILABLE CIRCUMSTANCE: NIL**REFERENCES**

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