FORMULATION AND EVALUATION OF METFORMIN VEGAN GUMMIES FOR GESTATIONAL DIABETES

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by

SHIVANGI

(Enrollment no. 220227056084788)

Under the Supervision of

Prof. (Dr).Amarjeet Singh
Supervisor

Mrs. Roshan Zehra
Co-Supervisor

Innovative College of Pharmacy, Greater Noida

to the

Faculty of Pharmacy

DR. APJ ABDUL KALAM TECHNICAL UNIVERSITY
(Formerly Uttar Pradesh Technical University) LUCKNOW

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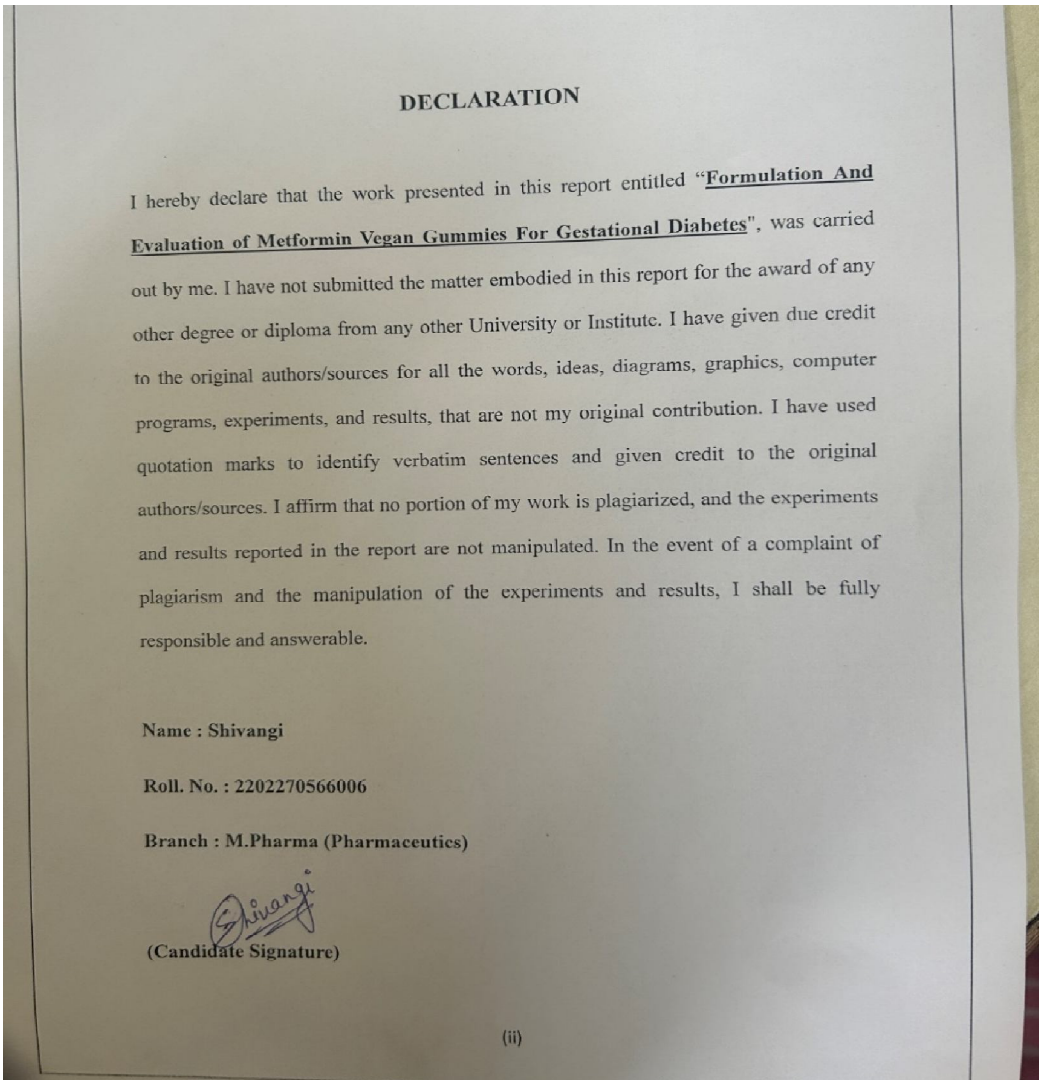

DECLARATION

I hereby declare that the work presented in this report entitled "**Formulation And Evaluation of Metformin Vegan Gummies For Gestational Diabetes**", was carried out by me. I have not submitted the matter embodied in this report for the award of any other degree or diploma from any other University or Institute. I have given due credit to the original authors/sources for all the words, ideas, diagrams, graphics, computer programs, experiments, and results, that are not my original contribution. I have used quotation marks to identify verbatim sentences and given credit to the original authors/sources. I affirm that no portion of my work is plagiarized, and the experiments and results reported in the report are not manipulated. In the event of a complaint of plagiarism and the manipulation of the experiments and results, I shall be fully responsible and answerable.

Name : Shivangi

Roll. No. : 2202270566006

Branch : M.Pharma (Pharmaceutics)

Shivangi

(Candidate Signature)

(ii)

Formulation And Evaluation of Metformin Vegan Gummies For Gestational Diabetes

Shivangi

'ABSTRACT'

This study aimed to develop and assess the suitability of pectin-based gummies as a vehicle to deliver metformin in Pregnant women. Metformin is very popular among diabetic patients for treating type-2 diabetes mainly in patients who are overweight. On the other hand, Pectin is a natural polysaccharide obtained from fruits and it is here chosen as a base as a gelling agent to replace gelatin, an animal-deprived agent. Pectin is chosen to make formulations for people who follow vegan dietary practices. Metformin was incorporated into pectin-based gummies which will offer an alternative and novel dosage form. Both Pectin and Metformin have a role in glycemic control. and their potential as an adjunct therapy in Diabetes management.

Formulation parameters thatinvolved Pectin concentration, Metformin dosage, incorporation of flavoring agents, and masking bitter taste of metformin were systematically optimized to achieve desirable optical sensory attributes and pharmaceutical characteristics. Various evaluation parameters were performed such as Physical characterization, drug content uniformity, In-vitro studies, and Stability assessment to check their quality and performance. The synergetic effect and potential benefits of the combined use of Metformin and Pectin (base) were studied. The evaluation part of gummies concludes the better stability, quality, and performance to support their potential translation into clinical practice.

The results concluded that it is feasible to produce Metformin-loaded pectin gummies, with acceptable organoleptic properties, uniform drug distribution, and sustained drug release profile. Besides, Stability studies data concluded that the formulated gummies showed satisfactory stability under accelerated storage conditions. Importantly, the combined use of pectin and metformin not only expedites the development of vegan dosage forms but also gives the potential benefits which are improved patient compliance, reduced gastrointestinal side effects, and enhanced drug bioavailability.

The development of gummies underscores the potential of vegan metformin gummies as a convenient, palatable, and potential therapeutic efficacy alternative for diabetic patients who are adhering to vegan diets, with the benefits of combined use of pectin-based formulation and metformin therapy.

Future investigation on Vegan Metformin gummies should be more focused on advancing clinical translations, formulation optimization, combination therapies, personalized dosage studies, in vivo studies, alternative applications, consumer acceptance, and regulatory approval to contribute to improved diabetic management and patient outcomes.

Keywords: Metformin, Convenience, Pectin, Gestational diabetes.

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SHIVANGI

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATION

WHO – World Health Organization

GBD- Global Burden of Disease

T1D- Type 1 Diabetes

T2D- Type 2 Diabetes

PCOS- Polycystic Ovary Syndrome

IR- Insulin Resistant

DPN- Diabetic Peripheral Neuropathy

GLP- Glucagon-like peptide

SGLT-2 inhibitors- Sodium-glucose transport protein 2 inhibitors

GRAS- Generally Recognized as Safe

Conc. – Concentration

w/w- Weight by weight

CHAPTER 1
INTRODUCTION

1 INTRODUCTION.

1.1 Overview and Origin of Diabetes Mellitus

Origin of diabetes can be traced back a thousand years ago. While our understanding of the disease has evolved significantly over time, historical records and archeological shreds of evidence suggest that diabetes has been a recognized medical condition for centuries.

Ancient Civilization:

Diabetes was described in ancient civilizations such as Egypt, Greece, India, and China. Ancient Egyptian manuscripts dating back to around 1500 BCE mention a condition that was characterized by excessive urination, a symptom linked to diabetes Vecchio et al[48].

Similar Ancient Greek physicians such as Hippocrates and later Aretaeus of Cappadocia (1st Century CE) described a condition that they called 'Diabetes', Referring to a condition in which a large amount of urine passes from the body, emaciation, and weakness.

Early Medical texts:

The expression "Diabetes" is gotten from the Greek word for "siphon," and that signifies "to go through.," which aptly describes the condition's hallmark symptom of excessive urination. Ancient medical texts, including those of Indian Ayurveda and Chinese medicineAhmed Awad[1]. They also made references to a disease with symptoms similar to Diabetes.

Early Understandings:

Before the discovery of Insulin, the treatment of diabetes was limited and somewhere ineffective. Ancient remedies included dietary modification, herbal concoctions, and even crude surgical interventions to relieve symptoms of diabetes.

Evolution of Medical Knowledge:

The advancement in medical science and understanding of diabetes was seen from the 19th and early 20th centuries. Researchers began to recognize the role of the pancreas in diabetes, leading to experiments aimed at understanding its function.

In 1889, German physiologist Oskar Minkowski and Austrian physician Joseph von Mering made a key discovery when they found that removing the pancreas from dogs caused them to develop diabetes symptomsAhmed Awad[1]. This made to comprehend the pancreas assumes a pivotal part in controlling glucose levels

Leveraging this understanding, the scientist of Canada Frederick Banting and their colleague Charles Best conducted pivotal experiments that ultimately resulted in the isolation and purification of insulin. This pancreatic hormone is essential to regulate blood glucose homeostasis.

Discovery of Insulin

Discovery of insulin represents one of the most pivotal advancements in the history of diabetes research. In the early 20th century, significant contributions were made by researchers including Frederick Banting, Charles Best, and John Macleod. Their systematic experiments culminated in the successful isolation and purification of insulin, a peptide hormone generated by the pancreatic islets, which is crucial for the regulation of blood glucose homeostasis. A major turning point in the treatment of diabetes was the breakout in 1921-1922, particularly for the type-1 diabetes patients who require insulin therapy to survive.

Continued research and Advancements:

Throughout the 20^{th} and 21^{st} centuries, advancements in medical terminology, pharmacology, and understanding of the disease have led to improved treatments and management of the diabetes mechanism, risk factors, and treatment options.

1.2 HISTORICAL PERSPECTIVES ON DIABETES

The Ebers Papyrus, originating back to 1550 BCE, was discovered in a tomb in the Thebes region of upper Egypt in 1862 and subsequently named in the honor of Egyptologist Georg.Ebers. Ahmed Awad[1]. This ancient documentIncludes detailed descriptions of numerous pathologies, including condition characterized by excessive urination, which is presumed to be diabetes. The Egyptians recommended several therapies for this condition, includes a decoction of bōs, wheat and earth Ahmed Awad[1].

In ancient India, there was an early recognition of the relationship between diabetes and elements such as heredity, over weight, bad lifestyle, and the diet. Indian practitioners advocated for the use ofFreshly harvested grains and bituminous compounds containing benzoates and silica were used as therapeutic agents for diabetes. The first recorded Correlation of polyuria with saccharine substancesappearedDocumented in Indian literature from the 5th to 6th century CE., attributed to Sushruta, a prominent Indian-physician.

Additionally, the Greek physician Aretaeus of Cappadocia provided a vivid description of diabetes, referring to it as a "wonderful affection" Characterized by the degradation of body tissues into urine.

Ancient times-

The earliest recorded mention The documentation of diabetes dateback 1500 BCE in Ancient- Egypt.Theword "diabetes" is generatedfrom the Greek word "siphon," which means "to pass through.," accurately depicting the excessive urination that characterizes the condition. They also made references to a disease with symptoms similar to Diabetes and recommended treatments such as exercise, dietary modifications, and herbal remedies but they didn't understand the causes behind them.

Middle-Ages-

During the Middle-Ages diabetes was referred to as "pissing evil". Throughout middle era, Diabetes was often fatal, with patients experiencing severe symptoms and a short life expectancy. Physicians recommended various treatments, including dietary restrictions and herbal remedies, but they had limited success.

17th& 18th Century-

In the 17th century, the English physician Thomas Willis observed the sweet taste of urine in diabetic patients, indicative of elevated glucose levels. He subsequently identified diabetes as a metabolic disorder. This observation led to the ground state of the disease for future research and understanding.

In the 18th century, experiments involving the analysis of diabetic urine initiated the discovery of sugar presence in the urine of diabetic patients.

19th Century-

In the 19th century, pivotal advancements in diabetes research emerged, notably through the work of German scientists Oskar Minkowski and Joseph von Mering. Their 1889 study demonstrated that surgically removing the pancreas from dogs induced diabetes mellitus. This groundbreaking experiment elucidated the pancreas's crucial role in glucose metabolism and insulin production, establishing a foundational understanding of diabetes etiology. Minkowski and von Mering's findings marked a significant milestone in medical science, linking pancreatic function directly to the pathogenesis of diabetes mellitus.

20th Century-

In the 1920s, Frederick Banting and Charles Best, along with their research team, made a transformative breakthrough in the therapy of diabetes with the discovery of insulin. Insulin injections became a life-saving therapy for patients with type-1 diabetes which increases their life expectancy. Insulin extracted from the animal pancreas became the first effective treatment for type-1 diabetes.

Throughout the 20th century, researchers made further discoveries about the mechanism of diabetes and other treatments like oral medications for type-2 diabetes such as sulfonylurea, and biguanides.

21st Century-

Continuous research was observed in the 21st century including advances in understanding genetics and environmental risk factors. The researchers continued progress with a focus on understanding the genetic, environmental, and lifestyle factors contributing to the disease. Modern advancements in diabetes management encompass a range of sophisticated technologies, including continuous glucose monitoring (CGM) devices and insulin pumps, and closed-loop systems, often referred to as artificial pancreas systems.

Ongoing research on Pancreatic islet cell transplantation and stem cell therapy aims to develop potential cures for diabetes.

1.3 INTRODUCTION OF DIABETES MELLITUS

Diabetes Mellitus(DM) constitutes a chronic metabolic condition characterizes by persistent hyperglycemia, results from inadequate insulin production or impaired insulin_ action within the body. It encompasses a spectrum of autoimmune, metabolic, and genetic conditions. Globally, the prevalence of diabetes has escalated, with estimates from the World Health Organization (WHO) indicating over 400 million individuals affected worldwide. Recent data fromWorldwide Disease Burden, Injury, and the Global Burden of Disease (GBD) 2019 studyunderscored diabetic as the 8thleading cause of combined mortality and, disability globally, impacting nearly 460 million people across various age groups in 2019. The International Diabetes Federation's 2021 figures suggest a further increase to 537 million individuals affected globally.

Diabetes significantly amplifies the risk of ischemic heart disease and stroke, ranked as the foremost and second leading contributors to the global disease burden according to GBD 2019 Egan & Sean[18] Despite global efforts, projections from 2016 the NCD Risk Factor Collaboration (NCD RisC) study indicate minimal progress toward achieving targets to mitigate the escalating prevalence of diabetes by 2025, particularly among women Ong et al[34] This underscores the urgent need for comprehensive strategies to address the social, health, and economic implications posed by the burgeoning diabetes epidemic worldwide.

1.3.1 Types

Diabetes mellitus encompasses several distinct types, primarily divided into type1 diabetes(T1D), and type2 diabetes(T2D), which represents predominant forms.

1.3.1.1 Type1 diabetes(T2D),Also referred to as insulin-dependent diabetes or juvenile-onset diabetes, typically... manifests during childhood or adolescence. It results from the immune system annihilation of. pancreatic β cells, which are answerable for delivering insulin. The precise etiology of type 1 diabetes remains elusive, although genetic predisposition and environmental triggers are implicated. This condition constitutes approximately 5-10% of diagnosed diabetes cases globally Kaul et al[28] The autoimmune process leads to a severe insulin deficiency, necessitating lifelong insulin therapy to manage blood glucose levels effectively.

Pathophysiology-

The susceptibility of pancreatic beta cells to stress induces the formation of neoantigens, which trigger an immune response. This autoimmune process involves a series of molecular events leading to localized inflammation termed insulitis. Over time, this inflammatory process results in significant and persistent impairment or reduction in beta cell function or mass Del et al[15] In the initial stages, the recognition of autoantigens is limited, and mechanisms such as alterations in surface antigens may temporarily attenuate the autoimmune attack on pancreatic islets, thereby slowing down the destruction process. These immune-mediated dynamics

underscore the complex pathogenesis of type 1 diabetes, highlighting the interplay between genetic predisposition, immune dysregulation, and environmental factors within the onset and advance of the disease Atkinson, M.A[8]

Epidemiology-

Type1 diabetes(T1D) exhibits a gender predominance with a higher incidence in males, potentially influenced by estrogen's protective effects observed during puberty. In vitro studies have demonstrated that estradiol mitigates the impact of glucose by inhibiting the expression of endoplasmic reticulum stress markersKooptiwut et al[31]

1.3.1.2 Type2 Diabetes(T2D)

Type2 diabetes(T2D) represents a prevalent metabolic_disorder.

Type 2 diabetes (T2D), alternatively termed Non-Insulin-Dependent Diabetes Mellitus (NIDDM),is characterizes by the ability to manage glycemic levels through oral medications and lifestyle modifications rather than solely relying on exogenous insulin administration.

There are two main causes of T2D-

i) Impaired insulin secretion by pancreatic beta cells.
ii) Non-ability of insulin-sensitive tissues' responsiveness to insulin.

It can damage nerves, kidneys, heart, vasculature, and eyes. 90% of the cases of diabetes are of T2D. People are characterized by obesity or Increased body fat percentage, particularly centralized in the abdominal region.

Pathophysiology-

A glitch In the criticism circle between insulin activity and insulin emission, this outcomes in raised glucose level Stumvoll et al[45] Specifically, beta cell dysfunction diminished insulin-secretion and limits body's ability to regulate sugar level within physiological ranges

Insulin-resistance(IR) add to improved hepatic gluconeogenesis and diminished glucose take-up in skeletal muscle and fat tissue and the liver.The combined impact of IR and β cell dysfunction underscores the complex pathophysiology_of conditions like type2 diabetes mellitus(T2D) Galicia et al[21] When both Beta cell dysfunction and IR are present then it causes hyperglycemia which leads to T2D.

Epidemiology-

According to the International Diabetes Federation (IDF), diabetes cause 3.2million deaths and 463 million people between 20 to 79years of age were living with diabetes in 2019 Galicia et al[21].

Type 2 diabetes(T2D) susceptibility emerges from complex exchange between the hereditary inclination and the natural impacts. Hereditary component add to T2D risk through collaborations with ecological openings, for example, inactive way of life and fatty weight control plans.Variations in genetic backgrounds across different

ethnic groups contribute to distinct phenotypic expressions that predispose individuals to multiple risk factors, including insulin resistance, hypertension, and dyslipidemia.

IR-Insulin resistance refers to a condition where insulin-responsive cells exhibit reduced metabolic responsiveness to insulin, or systemically, where there is impaired or diminished response to circulating insulin concerning blood glucose levels Galicia et al[21].

Table 1.1. Divergence between T1D and T2D

	Type1 Diabetes(T1D)	**Type2 Diabetes(T2D)**
Diagnosis Age	Generally in Childhood and adolescence but in adults also sometimes	Usually post-pubertal, Common in adults to old age people
Diabetes in 1st degree relative	Unusual	Common
Severe osmotic symptoms/ Ketosis at diagnosis	Can occur	Rare
Markers of insulin resistance	Absent	Present
C-peptide assay	Absence	Present
Pancreatic Autoantibodies	Present	Absent

1.3.2 SYMPTOMS

Symptoms of Type-1 diabetes come quickly and are more severe. The conditions may prediabetic, gestational diabetes, or type-2 diabetes which depends on how much amount of high sugar level in the blood.

The general symptoms of T1D and T2D are-

1. Fall in weight.
2. Recurring urination.
3. Experiencing increased thirst beyond typical levels.
4. Tiredness and weakness.
5. Blurry vision.
6. Slow healing sores.
7. Presence of ketones in urine.
8. Irritation.
9. Lots of infections like in skin, gum, or vaginal infection.
10. Numbness in hands or feet.

1.3.3 RISK FACTORS

1.3.3.1 Risk Factors Involves in Type1 Diabetes(T1D)

a) Genetics- It plays a remarkable role in the cause of T1D. If any close member of the family like a sibling or parent has type-1 diabetes (T2D) then, the appearance of some specific genes in the body may cause type-1 diabetesPociot& Ake[38]

b) Autoimmune factor- T1D is considered to be an autoimmune disease. It means the immune systems have been attacking healthy cells. Certain factors such as exposure to some viruses, or infection may trigger an autoimmune response with a genetic predisposition.

c) Geography- In some research, it was found that type-1 Diabetes varies by geography, with high rates observed in countries farther from the equator. Sunlight exposure and vitamin D levels alsoit assume a vital part in the pathogenesis.

d) Environmental factors- The presence of a virus like enterovirus in the environment may trigger the auto-immune response that leads to type1 diabetes in susceptible personsAkerblom et al[2]

e) Age- It can manifest at any age, with two prominent peaks observed between 4-7 years and 10-14 years of age in children.

f) Race and ethnicity- Non- Hispanic white individuals have high chances of T1D than other groups.

g) Early diet- Some shreds of evidence show that the timing of the food plays ancruicial part in the development of Type1 Diabetes. Breastfeeding practices or certain foods such as high sugar, and high fats also affect the development.

1.3.3.2 Risk Factors Involved in Type-2 Diabetes Wu et al[50]

a) Obesity, characterized by an excess accumulation of body fat, particularly in the abdominal region, contributes to increased insulin resistance and impaired glucose metabolism.

b) Unhealthy diet- Increased consumption of processed foods, refined carbohydrates, sugars, saturated fats and low fiber fruits or vegetables increases the risk of Type-2 Diabetes. Poor diet causes obesity, hyperlipidemia, and insulin resistance.

c) Physical inactivity- Insufficient regular physical activity is linked with an elevated- riskof developing, type2 diabetes mellitus(T2D).Exercise helps in

the improvement of insulin sensitivity and glucose uptake of cells which helps in reducing the risk of diabetes.

d) Family History(FHx)- The cases of type2 diabetes mellitus(T2D) in the family may contribute to passing through genetics and cause the disease. Lifestyle factors also contribute to the familial clustering of diabetes.

e) Age- Individuals aged 45 years and older are at heightened risk for type 2 diabetes mellitus (T2D) due to age-related physiological changes that affect insulin secretion and body composition, leading to insulin resistance.

f) Ethnicity- According to the CDC, diabetes is highly present in black, Hispanic, American Indian, Alaska, Alaska native countries, and some Pacific Islander and Asian American Communities.

g) Gestational diabetes-Lady who have the accomplished gestational_diabetes or who have been given convey a child weight more than 9pounds are at expanded hazard of creating type2 Diabetes mellitus (T2D) resulting throughout everyday life.

h) Polycystic Ovary Syndrome(PCOS)- PCOS is hormonal turmoil in ladies confronted irregular_menstrual cycles, hyperandrogenism and the presence of ovarian sores. Lady with PCOS are at a raised gamble of insulin-opposition and, type2 diabetes mellitus(T2D).

i) Dyslipidemia- Raised degrees of low thickness lipoproteins(LDL) cholesterol and, fatty substances, alongside diminished degrees of highdensity lipoprotein(HDL) cholesterol, are in many cases seen in insulin opposition individual and type2 diabetes mellitus(T2D). This dyslipidemia essentially raises the causing of cardiovascular disease(CVD), addressing a significant complexity in the diabetic populace.

j) Hypertension- Dyslipidemia is a frequent characteristic of type2 diabetes mellitus(T2D), often sharing risk factors such as obesity and physically inactive.

1.3.4 CAUSES

1.3.4.1 Insulin insufficiency

ThisCondition characterized by pancreatic insufficient insulin production., is the primary cause of type1 diabetes mellitus(T1D). The insulin deficiency arises fromThe immune system's targeting of the beta cells in the pancreas responsible for insulin production.

Without sufficient insulin, cells cannot absorb glucose effectively from the bloodstream which causes high blood glucose levels.

1.3.4.2 Insulin Resistance

Insulin-opposition is an ailment characterized through a change in portion reaction bend, bringing about a diminished degree of the organic reaction to insulin. It is the essential etiological calculate the causing of type2 diabetes mellitus(T2D). Hindered insulin reaction can appear across the total assortment of insulin fixations.. or then again explicitly on low-conc.. of chemical Taylor et al[46]

Even though the pancreas may produce insulin, the pancreas does not show any response to it. It happens when cells in the muscles, fat, and liver an unresponsive to insulin. This leads in response to an elevation in the sugar range in the blood because glucose remains in the bloodstream rather than being taken up by the cells for energy.

Insulin resistance is associated with obesity, physical inactivity, due to certain medications, and genetic predisposition.

Other causes involved are lifestyle habits, eating habits, Physical inactivity, genetic factors, Hormonal Imbalance, Autoimmune disease, Pancreatic damage, or genetic mutations.

1.3.5 COMPLICATIONS

Diabetes affects many organs in the body and leads to significant complications.

Complications arising from diabetes are classified as a) Micro vascular

b) Macro vascular

Microvascular complications encompass damage to various small blood vessels in the body, including those affecting the nervous system(neuropathy), renal system(nephropathy) and eyes (retinopathy).

Macrovascular complications encompass disorders affecting large blood vessels in the body, including cardiovascular disease (CVD), stroke, and peripheral vascular disease(PVD).

Cardiovascular disease(CD) and stroke

Cardiovascular disease(CD) is responsible for approximately 65% of mortality in individuals with diabetes. Moreover, people affected by diabetes faces a two-four times higher risk of developing stroke compared to those without diabetesPandey et al [17]The precise role of hyperglycemia in contributing to cardiovascular complications among individuals with diabetes remains uncertain and complex.

Peripheral arterial disease(PAD)

Peripheral arterial disease(PAD) arises from the thinning of bloodvessels that supply blood_to the arms, legs, kidneys, and, abdominal organs. Risk factors for PAD include advanced age, prolonged duration of diabetes, and the presence of neuropathy[35]Acc. to the The National Center for Health Statistics and hospital discharge recordsrate for Peripheral arterial disease(PAD..) as the first_diagnosis is higher in men compared to women and increases with advancing agePandey et al[17]

Retinopathy

Diabetes can causes damage the blood vessels present in the retina, which may cause diabetic retinopathy. It results in over 10,000 cases annually. The prevalence of visual impairment among diabetic people increases with age. Ninety percent of blindness attributable to retinopathy occurs among diabetic individuals may be preventable with early detection and timely treatment.

Nephropathy

Diabetes is a leading cause of kidney diseases. Diabetic Nephropathy is persistent proteinuriain patients lacks in urinary tract infections or other comorbid conditions. In T1D, the progression of the Nephropathy is typically a late-stage complication but In T2D Nephropathy may be evident at the time of diagnosis.
The aetiology of diabetic nephropathy is not completely understood.

Neuropathy

Peripheral Neuropathy can affect the nerves that control sensation, movement, and organ function. It is a prevalent complication that is estimated to impact 30% to 50% of individuals diagnosed with diabetes.Pepatheodorou et al[35] Individuals with diabetic peripheral neuropathy(DPN) are at a high risk for foot ulcers and subsequent lower extremity... complications.

Gastroparesis

Elevation of blood glucose levels can impair the nerve function involved in the gastrointestinal system, causing gastroparesis. It is a condition in which the stomach takes a longer duration to get empty than usual.

Skin Complications

Diabetic people are more prone to various skin-related issues like bacterial or fungal infections, itching, and delayed wound healing

Foot Complications

Diabetes increase the cause of foot ulcer, and the infections, and in the severe cases, it can lead to amputation.

1.3.6 DIAGNOSTIC METHODS

1.3.6.1 High Blood Sugar

a) The fasting glucose (FPG) test

The fasting Plasma Glucose (FPG) analytic evaluates the glucose conc. in the blood after a time of fasting. After the 8 hours of fasting, this test is finished.

b) The Random Glucose (RPG) test : In this diagnostic procedure, the conc. of Blood sugar levels in blood of the patient are measured regardless of when you ate last. This test can be done anytime.[3]

c) The Oral Glucose Tolerance (OGT) Test

In this diagnostic procedure, after overnight fasting the blood sugar level are initially measured, after which the the patient consume glucose solution and again the blood glucose level is diagnosed after 2 hours. If the patient has a high blood glucose level then he has diabetes. It is more costly than FPG.

d) Urinalysis

In this diagnostic procedure, the presence of glucose in the urine is tested.

1.3.6.2 Increased HbA1c

This diagnostic procedure measures the avg. blood sugar levels in the blood from the past two- three months. This test not accurate in some health conditions such as anemia, 2nd or 3rd trimester of pregnancy, or another problem in the blood.[41]

A patient can eat or drink before this test. The doctor will give the results of this test in percentage. A higher percentage means high blood glucose levels. HbA1c level is not affected by short-term lifestyle changes. HbA1c accurately reflects long-term glycemia.

Table.1.2Results to determine Blood glucose levels

Diagnosis	HbA1c	Fasting Plasma Glucose(FPG) Test	Oral Glucose Tolerance(OGT) Test	Arbitrary Plasma Glucose Test
Within normal limits	under 5.7%	99mg/ dL or less	139mg/ dL or less	-
Within Prediabetes limits	5.7% to 6.4% range indicative	100 to 125mg/dL range indicative	140 to 199mg/dL	-
Within	6.5% range	126mg/dL or	200mg/dL range	200mg/dL or

Diabetes limits	indicative or more	more	indicative or above	more

Other methods involved-

Glycate Albumin test-

This diagnostic procedure calculate the amount of glycate albumin in the hemoglobin of blood and checks average ,blood glucose levels from the preceding 2 - 3 weeks.

C-peptide Test-

This diagnostic test finds the levels of C-peptide in the blood which is the by-product of insulin production. It measures the amount of insulin produced by the body.

1.3.7 TREATMENTS

1.3.7.1 Lifestyle Changes:

Lifestyle changes are very important to manage diabetes by managing blood sugar levels. It also aimed at enhancing the overall health. Includes-

1) Healthy Eating Habits: Chong et al[13]

- Balanced Diet- Eat food that is dense in nutrients and fiber such as fruits, green vegetables, whole grains, and healthy fats.
- Portion Control- Avoid overeating and manage the total calorie content in a day.
- Do not take processed food- Processed foods are high in sugars and preservatives, it is stored in the body as bad fat. It contains refined oil and carbohydrates.
- Limit sugar- Do not take high sugary foods or avoid the consumption of sugar.
- Carbohydrate management- Only choose complex carbohydrates with a low glycemic index to regulate the blood sugar levels and also monitor the carbohydrate intake.

2) Regular Physical Activity:

- Strength training- Doing strength training twice a week will build muscle mass, it will regulate blood sugar levels, and also improve the overall metabolism of the body.
- Aerobics- Aerobic activities include jogging, swimming, walking, running, cycling, or dancing.It will decrease blood glucose levels and enhance insulin sensitivity..

- Balancing and Flexibility exercises- To improve flexibility, do yoga or tai chi. It will also improve overall well-being.

3) Stress management:

- Stress reduction Techniques- Stress increases the adoption of sugar in the blood. To manage the stress level, deep breathing, meditation, and yoga, will help in controlling the blood sugar level.
- Healthy Coping Mechanisms- Participating in leisure activities, socializing with family and friends, taking supportive intervention from a therapist or counselor can deal with the stress.

4) Weight management:

- Healthy weight loss- Healthy weight is achieved by the combination of a healthy diet and physical exercises. It will improve insulin sensitivity and complications associated with diabetes Chong et al[13]
- Set realistic goals- Engaging in drastic or fad diets is not good. Only set achievable goals and focus on sustainable lifestyle changes the weight.

5) Regular glucose monitoring:

- Regular check-ups- Attend scheduled blood tests to monitor diabetes and its progression, vaccination plans or receive necessary screenings.
- Blood glucose monitoring- Real-time glucose monitoring is very effective in critical cases. As recommended by the healthcare providers, track progress and make adjustments in the treatment plans.[13]

1.3.7.2 Medications:

Medications can only maintain the blood glucose level not fully treat diabetes.

Medications for type-1 diabetes

a) Insulin- Insulin is the most common medication to complete the insulin need in type-1 diabetic patients. It is administered through infusion in the blood Katsarou et al[27]

Short-acting insulin: It reaches the blood after 30min of administration and peaks 2-3 hours afterward. Like as Humulin ru-10 and Novolin r FlexPen, Novolin reliOn and Novolin r flexPenreliOn.

The Rapidacting insulin: It reaches bloodstream after 15min of administration and peaks 1-2 hours afterward. Incorporate Breathed in insulin (Afrezza), Insulin as part, Insulin glulisine, Insulin lispro, Insulin lispro-aabc.

Intermediateacting insulin: It typically exerts its effects approximately 2-4 hours post-administration, with an average peak action observed around 12 hours. Include- Insulin Isophane.

Long-acting insulin: It works about 24 hours or more after use. It stabilizes in the bloodstream longer without a peak. Like as Insulin degludec, insulin detemir, insulin glargine, insulin glargine-yfgn, and conc.standard insulin

b) Mix insulin: It incorporates insulin aspart Protamine or insulin aspart 70/30 and Insulin isophane or standard insulin 70/30.
c) Amylinomimetic injectables- It is used before meals. Pramlintide is an amylinomimetic. It helps in lowering the empty time of the stomach.It also decreases postprandial glucagon secretion. This will help with blood sugar levels.

Medications for type-2 diabetes Hu & Weiping[23]

a) Alpha-glucosidase inhibitors- It is taken before the meals.
Ex, Acarbose, Miglitol.
b) Guanides- It helps in decreasing the making and absorption of glucose.
Ex, Metformin.
c) Dopamine-2 agonist- It prevents insulin resistance.
Ex, Bromocriptine.
d) Dipeptidyl peptidase-4 (DPP-4) inhibitors- It helps the pancreas to make more insulin.
Ex, Alogliptin, Linagliptin, Sax gliptin.
e) GLP-1 receptor agonist- It helps decrease appetite, and slow stomach emptying which helps in good absorption of nutrients.
Ex, Dulaglutide, Exenatide.
f) Meglitinides- They help the body to release insulin.
Ex, Repaglinide, Nate glinide.
g) SGLT-2 inhibitors- They prevent the kidneys from holding on to glucose.
Ex, Canagliflozin, Dapagliflozin.
h) Sulfonylureas- They stimulate The pancreas, facilitated by beta cells, Participating in this process will make the body produce additional insulin.
Ex, Glimepiride and Glipizide.
i) Thiazolidinediones- It works by inhibiting gluconeogenesis in the liver. It additionally helps the adipocytes to usage the enhances insulin sensitivity.
Ex, Rosiglitazone, Pioglitazone.

1.3.8 PREVENTION

Type1 Diabetes mellitus(T1DM) is not preventable ,and in some instances of type2 diabetes mellitus such as genes or age can’t be preventable. Yet many other diabetes risk factors are preventable.

Primary Prevention

It aims to prevent the onset of diabetes in individuals who do not have the condition.

- Health Prevention-
  A healthy lifestyle is promoted through education and awareness campaigns about the importance of a balanced lifestyle, Physical activity & weight management.
- Community interventions-
  Healthy eating programs, physical activity promotions in schools & workplaces, and policies to create environments conducive to healthy behaviors are implemented through community-wide interventions.
- Screening & Early detection-
  Identifying individuals at risk for diabetes through screening tests and intervening with lifestyle interventions before the onset of the disease.

Secondary prevention

Its goal is to identify and manage diabetes during its initial stages to mitigate or postpone complications and progression to more severe forms of disease.

- Screening & Diagnosis-
  Regular screening of diabetes & prediabetes in high-risk individuals, those with family history, obese or overweight, and those with certain ethnic backgrounds.
- Early intervention-
  Dietary changes, exercise programs, weight management, and if necessary, medications forIndividuals diagnosed with prediabetes are targeted todelay/forestall the beginning of type2 diabetes through early intercession measuresLaaksonem et al[33]
- Monitoring & Management-
  Continuous observing of glucose levels and other wellbeing boundaries to detect and manage diabetes complications early andmitigate the risk of chronic complications.

Tertiary Prevention

It aims to prevent the onset of complications associated with diabetes & Increases the life's quality for individuals already diagnosed diabetes.

- Comprehensive Diabetes Care-
  It includes regular health check-ups, medication management, education on self-care practices, and access to diabetes education and support groups.
- Management of Complications-
  Early detection and management of diabetes-related complications through regular screening, lifestyle modifications, medication management, and referral to specialists when needed.
- Rehabilitation & Support services-

Physical therapy & Occupational therapy and psychosocial support to diabetic individualsto assist them in managing the physiological, emotional, and social challenges linked with the condition.

1.3.9 SOCIAL & CULTURE

Diabetes Mellitus is a lifestyle disorder. Economic, social & cultural resources influence health capability & dietary management. Weaver et al49]

- **Stigma & Misconception**- Type2 diabetes is related with a lifestyle such as poor diet and lack of exercise. So, In some cultures, it is a stigma that leads to a feeling of shame or blame among those diagnosed with diabetes. This is the main reason behind the increase in type-2 diabetes. In some cultures, there may be a perception that diabetes is a punishment for moral failings or lack of willpower.

- **Family Dynamics & Support**- In some cultures, people might be resistant to changes in traditional eating habits making management more challenging. Conflicting cultural beliefs, within families such as traditional remedies versus modern remedies, can create tension sometimes and affect the management of the condition.
- **Diets & Eating habits**- Cultural diets and eating habits can lead to diabetes. A diet rich in carbohydrates or sugar can cause diabetes. The traditional diets are rich in fruits, vegetables, and whole grains are perfect for managing the condition of diabetes. Traditional dishes, cooking methods, and eating habits are often passed to the generations and this plays a crucial role in social gatherings and celebrations. For diabetes personnel, navigating personal norms around food can be challenging.

- **Healthcare access & beliefs**- Some communities have limited access to education, screening, and treatment for diabetes. Cultural beliefs about medication, alternative therapies, and healthcare providers can influence diabetes management decisions. Traditional medical practices, herbal remedies, and alternative therapies may coexist alongside modern medical treatments.

- **Religious practice & Fasting**- For diabetic patients, fasting can be a challenging aspect. Careful planning and coordination with healthcare providers are needed if they want to indulge in any religious practices. Healthcare providers need to respect and acknowledge cultural beliefs while providing evidence-based care.

- **Community Support**- Many communities have support groups, cultural groups, or advocacy focused on diabetes. These groups can help in providing

resources, and education, for diabetic people. They also work to raise awareness, reduce stigma, and advocate for better access to healthcare services. These networks can help individuals feel understood, accepted, and empowered to manage their diabetes within the context of their cultural identity.

It requires healthcare providers to recognize the diversity of cultural backgrounds and experiences among people with diabetes and to tailor care plans accordingly.

1.4 INTRODUCTION TO GESTATIONAL DIABETES

Gestational Diabetes-Mellitus(GDM) is portrayed by improves glucose levels analyzed during..., the second or third trimester of pregnancy, without meeting the criteria for overt diabetes outside of pregnancy..

It occurs in one of the seventh pregnancies worldwide Immanuel & David[25](GDM) is currently the most prevalent complication of pregnancy. Even overt diabetes in young women is increasing.

It is advised that all pregnant women undergo testing starting around 24–28th week of pregnancy. Gestational Diabetes-Mellitus(GDM) is typically analyzed during the... second or third trimester because of raised degrees of insulin-adversarial chemicals during this period. Following pregnancy, around 5-10% of ladies analyzed, with GDM are hence distinguished to have an other type of diabetes, most usually type2 diabetes mellitus(DM).

Gestational diabetes is manageable with comprehensive medical oversight during pregnancy. While it may resolve after childbirth, untreated gestational diabetes can pose health risks to both the fetus and mother.

1.4.1 Symptoms

- **Increased thirst**- Feeling of extreme thirst and need more to drink than usual.

- **Frequent urination**- Need to urinate more frequently especially at night than usual.

- **Fatigue**- After getting enough rest, the body feels more tired than usual.

- **Blurred Vision**- Vision may become blurred and feel uneasy in seeing things.

- **Nausea and vomiting**- It is ubiquitous in pregnancy. Some women may experience nausea & vomiting, like morning sickness.

- **Unexplained weight gain or loss-** Without a change in the diet and usual activity, there is an increase in the weight or loss of weight.

- **Increased hunger**- Feeling more hungry than usual and eating frequently. It is also the reason for more weight of the bay.

1.4.2 Causes

The precise causes of gestational diabetes are not fully known but several factors can be the reason.

- Hormonal Change- Some of the hormones that are produced at the time of pregnancy can disrupt the action ofinsulin signaling, resulting in insulin resistance. Due to this, body cells can't respond to insulin which causes gestational diabetes.

- Insulin resistance- As pregnancy progresses, the mother's body becomes more resistant to insulin.This resistance diminishes abilities of insulin to effectively regulate blood sugar levels, which leads to elevated blood sugar levels.

- Genetic- Women with a familial predisposition of diabetes are prone to developing gestational diabetes. Genetic factors implicated the production of insulin resistance.

- Age- Women especially beyond a certain age of 35, are at an elevated risk of developing gestational diabetes. As the age grows, the woman becomes less sensitive to insulin.

- Obesity- Being obese is very risky for women at the time of pregnancy. Excess weight can contribute to insulin resistance.

- Nationalities including African Americans, Hispanic Americans, Local Americans, and Asian Americans are show a higher powerlessness to creating gestational diabetes.

- Previous Gestational diabetes(GD)- Women with history of gestational diabetes in a prior pregnancy have a chance to develop again in the next pregnancy.

- PCOS- Women diagnosed who have Polycystic Ovary Syndrome(PCOS)are at elevated risk of insulin-resistance, thereby increasing susceptibility to gestational diabetes.

- Way of life A stationary way of life, for example, an absence of active work adds to disabled insulin responsiveness and expands the improvement of gestational diabetes.

- Poor diet- A diet high in carbohydrates and sugars contributes to induces insulin resistance and promotes weight gain which induces the chance of gestational diabetes as well.

1.4.3 Usual Onset

Gestational diabetes typically manifests during the second or third trimester of pregnancy, around 24^{th} to 28^{th} week. This happens because to organ that connects the baby to the mother's uterus, begins producing hormones that start interfering with the mother's insulin action Immanuel & David[25]

During the pregnancy, the placental hormone leads to insulin resistance in the mother's body. As a consequence, the body's cells exhibit decreased responsiveness to insulin, leading to elevated blood sugar levels. increase which causes gestational diabetes.

The onset varies from woman to woman, some women may develop earlier in pregnancy and some may later. In some cases, the woman may have undiagnosed diabetes before the pregnancy and the hormonal change in pregnancy exacerbates the condition leading to gestational diabetes.

Pregnant women need to undergo regular screening for gestational diabetes typically occurs between the 24^{t} and 28^{t}week of pregnancy, to detect the condition early and treat it effectively. Early detection and management can reduce the likelihood of complications for the mother as well as the baby.

1.4.4 Risk Factors

The primary risk variables of Gestational Diabetes incorporate high level maternal age, improves Weight Index(BMI), and a past filled with Gestational Diabetes Mellitus (GDM), among other factors. Women with Gestational Diabetes Mellitus (GDM) are at improved hazard of stoutness, metabolic condition, and Type2 Diabetes, sometime down the road. what's more, their children in later lifeKouhkan et al[32]

Metabolic disorders and genetic predisposition are the most common risk factors among Asians to cause GDMKouhkan et al[32]

Some other factors are:

a) PCOS
b) Obesity
c) Previous history of Gestational diabetes with the first baby over 9 pounds.
d) Genetics
e) Older than 25 ageduring the gestational period.

Excess body weight or obesity during pregnancy- It heightens the likelihood of developing gestational diabetes. Excess body weightcan result in diminished insulin sensitivity, which it impairs the body's ability to regulate glucose levels effectively Silva et al[43]

Family History of Diabetes- 1° relatives such as relatives or siblings with type2 diabetes, increase the risk of gestational diabetes. Genetics significantly influences insulin resistance and glucose imbalance.

Previous History of Gestational Diabetes or Heavy Baby- Those women who have a previous pregnancy with GDM will increase the chances of GDM in subsequent pregnancy. Those women who deliver babies having a birth weight exceeding 9 pounds have the chance of GDM in future pregnancies.

PCOS-It is a hormonal disorder that affects women of reproductive age, marked by irregular menstrual cycles., polycystic ovaries, and elevated androgen levels. Ladies with Polycystic Ovary Syndrome(PCOS) are at improved chance of insulin-obstruction &...likely to foster gestational diabetes.

Maternal Age- Age of 35yrs or more at the time of trimesters is linked with an elevated risk of gestational diabetes. As women age, their bodies become less efficient at processing glucose, which leads to higher insulin_resistance.

Ethnicity - Certain ethnic_groups have a higher risk_of GDM than others. Examples, are Hispanics, Native Americans, South Asians, etc. The reasons for these ethnic disparities are complex and may involve genetic, cultural, and lifestyle factors.

Lifestyle- Characterized by insufficient physical activity, is related with enhanced risk of type2 diabetes. Regular exercise enhances insulin sensitivity and promotes glucose metabolism of cells, which helps reduce the risk of diabetes Silva et al[43]

Certain Medical Conditions- Pre-existing medical conditions such as Hypertension, cardiovascular disease, and certain autoimmune disorders may increase the risk of GDM. These conditions disrupt normal metabolic processes and lead to insulin resistance.

Certain medications- Corticosteroids, used to treat asthma or autoimmune disorders can lead to GDM. These types of medications interfere with the insulin function and glucose metabolism.

1.4.5 Complications

Gestational Diabetes can lead to variouscomplications for both the maternal and fetal health. Proper management and monitoring are essential to minimize these risks Johns et al[26]

1.4.5.1 Complications to the Mother

a.) Type-2 Diabetes(T2D) risk
b.) Preeclampsia
c.) Gestational High Blood Pressure
d.) Cesarean Delivery
e.) Preterm Birth
f.) Polyhydramnios
g.) Urinary Tract Infection

1.4.5.2 Complications to the Baby

a) Macrosomia
b) Hypoglycemia
c) Respiratory Distress Syndrome Salzer et al[40]
d) Jaundice
e) Birth trauma

Maternal Complications:

Preeclampsia: Preeclampsia is a hypertensive disorder characterized by elevated blood pressure and organ damage, particularly affecting the kidneys. Lady have gestational diabetes are at raised chance of causing toxemia, which can bring about confusions like fetal development limitation and preterm birth.

Gestational hypertension: High blood pressure is very common during pregnancy, especially in woman with gestational diabetes.

Increase risk of cesarean:Woman with gestational diabetes are at risk of delivering macrosomic infants, which are babies with a birth weight > 90th percentile for their gestational age, increasing the chances of cesarean delivery. Surgical incisions are done around the abdominal wall and uterine wall.

Increased risk of type2 diabetes:A background marked by gestational diabetes(GD) essentially hoists the probability of creating type2 diabetes post pregnancy.

Risk of future gestational diabetes:Women with history of the gestational diabetesin one pregnancy are at an elevated risk of experiencing subsequent pregnancies.

Polyhydramnios: Excessive amniotic fluid creates pressure within the uterus and other organs which can lead to complications during delivery. It usually represents high-risk obstetrics conditions.

Urinary tract infections: It is the most commonly observed maternal infection. It usually suppresses the immune system and increases the chances of progression of acute cystitis, and renal abscess.

Preterm-Birth: Delivery before the 37 weeks of gestationhas been completed, is indeed a potential complication associated with gestational diabetes.

Fetal and Neonatal Complications:Sahneiver et al[42]

Macrosomia: Babies deliverby moms with Development diabetes are in danger of Macrosomic, which can lead to difficulties during birth and an increased risk_of birth injuries.

Hypoglycemia (low blood sugar): Babies deliversto the moms with Gestational diabetes encounters low glucose levels after conveyance due to the insulin creation is elevate in response to the mother's high blood sugar levels during pregnancy.

Respiratory distress syndrome(RDS) : Babiesbrought into the world by moms with development diabetes(GD) may has juvenile lungs, prompting respiratory trouble after birth.

Jaundice: Increased bilirubin levels in the baby's blood can lead to jaundice. Newborns that have jaundice have the same color of stools sometimes like that of without jaundice newborns.

Increased risk of stillbirth: While the overall risk of stillbirth is low, it may be slightly higher in pregnancies affected by gestational diabetes, especially if blood sugar levels are poorly controlled.

Birth Trauma:Any injury sustained by the baby during the birthing process, labor and delivery, In gestational diabetes the chances of birth trauma increases.

1.4.6 How to prevent Gestational Diabetes?

Some measures should be focused on to prevent gestational diabetes and complications for the mother and the baby.

Maintain Healthy Weight: Being obese increases the chance of Gestational Diabetes. It should be focused on that women maintain a healthy weight before thinking about conceiving and maintaining appropriate weight management strategies. Healthcare professionals can guide appropriate weight gaining for pre-pregnancy Body Mass Index(BMI). They can recommend the registered dietician or nutritionist to develop a personalized meal plan to support healthy weight during pregnancy.

Healthy eating habits: Women shouldFollowing a wellbalancediet rich in fruits, vegetables, whol_ grain andlean protein are essential.. Avoid excess intake of sugary products and processed food. Try to maintain a tailored meal plan. Including adequate fiber in the diet can also help regulate blood sugar levels. Additionally, focusing on lean sources of protein such as tofu, and legumes can help to stabilize blood sugar levels and maintain overall health silva et al[43]

Regular Physical activity: Physical activity is very crucial during overall pregnancy because it will improve the sensitivity of insulin and help to control weight gain.[30] Physical activity should be at least 30 minutes every day which includes swimming, brisk walking, or prenatal yoga. To start any exercise regimen, one should consult the doctor to ensure safety and appropriateness.

Blood sugar Monitoring: If there is any risk of gestational diabetes such as a family history or obese condition, the healthcare provider will surely advise regular blood sugar monitoring. This involves fasting blood sugar level in the morning and sometimes after meals with the help of a glucometer. This will help in the early detection of any abnormalities and timely prevention of complications.

Medication: In some serious cases of gestational diabetes it is necessary to take proper medications. Insulin and metformin are the commonly used medications to use during pregnancy because they are safeKenlleyMcauliffe[30] Patients should consult the doctor before taking any medication.

Stress Management:Chronic stress can adversely affect blood sugar levels and elevate the risk of gestational diabetes. Implementing Stress-decreasing procedures contemplation, yoga, and full breath works out can be beneficialmitigate these effects. They will promote relaxation, and improve overall well-being during pregnancy.

Avoid Smoking and Drinking: Smoking and alcohol consumption will promote the risk of gestational diabetes. Avoiding alcohol consumption entirely is necessary for the growth of a developing baby.

Proper Hydration: Maintaining a proper amount of hydration is necessary for overall pregnancy. This habit will help in maintaining blood sugar levels and support kidney functions. opt to drink water rather than any sugary drink or any beverages. Fruit juices and beverages will contribute to the fluctuation in blood sugar levels.

1.4.7 Postpartum Care

Postpartum care is very necessary to prevents the chances of Type2 diabetes. After the delivery, there are chances of type2 diabetes in mother as well as the baby.[19] Postpartum care is essential to monitor and manage any lingering effects of gestational diabetes.

Primary care follows: Postpartum primary care is demonstrated to improve rates of type-2 diabetes screening timely. Regular follow-ups to the doctor in the 12 months after delivery are crucialdamico et al[14]

Medications: The medications that are prescribed by the doctor should be taken on time for prevention. Insulin and metformin are the safest options as oral medications if the woman is facing diabetes complications after delivery. Metformin is also used to help in the weight management of obese. Without the consultation of a doctor, avoid any medication.

Breastfeeding Support: Breastfeeding has benefits for both the mother and the baby, helping regulate blood sugar levels. Lactation consultants provide support and guidance to ensure successful breastfeeding, which can aid in postpartum weight loss and improve maternal health.Woman having experienced gestational diabetes are strongly advised to breastfeed due to the numerous benefits it offers to both mother and infant Blumer et al[11]

Healthy lifestyle changes: Encouraging a healthy lifestyle is paramount in postpartum care. Adopting healthy eating habits such as vegetables, fruits, lean proteins, whole grains, and healthy fats. Portion control and monitoring carbohydrate intake help in the management of blood sugar levels.

Family Planning: Planning for future pregnancies involves optimizing health before conception to reduce the prevent the reoccurring of gestational diabetes and other complications. There are many chances of gestational diabetes in future pregnancies.

Regular Physical activity: Physical activity is very crucial after pregnancy also because it will improve the sensitivity of insulin and help to control weight gain Kennelly &Mcauliffe[30] Physical activity should be at least 30 minutes every day which includes swimming, brisk walking, or prenatal yoga. To start any exercise regimen, one should consult the doctor to ensure safety and appropriateness. Physical activity will manage the stress level also.

1.5 DIFFERENCE AND SIMILARITIES IN TYPE-2 DIABETES AND GESTATIONAL DIABETES

Difference between Type2 Diabetes and Gestational Diabetes

Table 1.3Difference between gestational diabetes and type2 diabetes

Gestational Diabetes	Type2 Diabetes
The regulation of blood sugar levels is impaired, and this condition occurs during pregnancy.	Blood sugar regulation is impaired due to insulin resistance, where cells exhibit reduced responsiveness to insulin's actions.
Only During pregnancy, there is reduced insulin production leading to impaired blood sugar regulation.	It can manifest in individuals across various demographics and is notably prevalent among those aged 40 years and older.
The primary etiology of gestational diabetes is attributed to hormonal changes during pregnancy, compounded by unhealthy lifestyle habits and obesity.	The main of type-2 diabetes is an unhealthy lifestyle, genetics, as well as lack of physical activity.
It is diagnosed when the sugar level goes above 140mg/dL after a meal and 100mg/dL before the meal.	It is diagnosed when the sugar level goes 200mg/dL after the meal and 100mg/dL before the meal.
The suffering women will feel thirst, tiredness, increased urination, and no other symptoms.	The individual may experience symptoms such as polyphagia (excessive hunger), polydipsia (excessive thirst), nausea, diabetic retinopathy (eye problems), and urinary tract infections, among other complications.
Blood sugar levels usually return to normal after delivery.	It is a chronic condition.

Similarities in Type2 Diabetes and Gestational Diabetes

Table 1.4 Similarities in Type2 Diabetes(T2DM) and Gestational Diabetes(GD)

Insulin resistance	In both conditions, the cells become insulin resistant, resulting in elevated blood sugar.
Risk factors	The Risk factors involved in both cases include obesity, sedentary lifestyle, lack of physical exercise, genetics, or ethnic groups.
Glucose Intolerance	In both cases, the patient experiences impaired glucose metabolism.

Management	Both conditions can be managed through lifestyle modifications. Some individuals need medication to control blood sugar levels in chronic conditions.
Complications	Some similar symptoms include hypertension, kidney problems, urine infections, cardiovascular disease, and neuropathy.
Screening	Screening methods involved in both cases include blood sugar tests.
Prevention	Both gestational diabetes and type2 diabetes can be prevented or, delayed through lifestyle- modifications such as a healthy diet, sleeping habits, stress management, fiber food, regular physical activity, and a diet low in refined sugars and oils.

1.6 PATHOPHYSIOLOGY OF GESTATIONAL DIABETES

Gestational Diabetes is arises from beta cell dysfunction exacerbated by chronic insulin resistance during pregnancy. This condition involves impaired function of beta cells in the pancreas and reduced responsiveness of tissues to insulin, crucial components in its pathophysiology. Multiple organs and systems are implicated in the development and impact of GDM, including brain, adipose tissue, liver, muscle, &the placenta, each playing roles in insulin regulation and glucose metabolism during pregnancy Plows et al[37]

Hormonal Changes:
During pregnancy, the placenta produces hormones necessary for fetal growth and development.Some hormones such as cortisol, estrogen, and placental lactogen can interfere with insulin function, leading to insulin resistance. Insulin resistance means the body cells become less responsive to insulin, necessitating higher insulin levels to maintain higher glucose levels.

β cell dysfunction:The main.. physiological roleofβ cells is to store and delivery insulin., a chemical vital for managing blood glucose levels. Beta cells unfunctional happens when these cells misfortune the capacity to precisely detects glucose fixations or, to deliver satisfactory measures of insulin in response to glucose upgrades.
The majority of genetic susceptibilities linked to Gestational Diabetes Mellitus(GDM) involve genes associated withFunction of β-cells.These incorporate K+ Voltage-gated channel KQT-like1 (Kcnq1) and gluco kinase(Gck). Minor... debilitations in βcell capability may just appear during times of metabolic pressure like as pregnancy, when increased insulin production and secretion are required to maintain normal glucose levels. These genetic factors contribute to the susceptibility to GDM by affecting the β-cells' ability to adequately respond to the increased demands of glucose metabolism during gestationPrentki et al[39] β-cells dysfunction is aggravated by insulin resistance. The direct contribution of glucose to βcell failure is called gluco toxicity.
Animal studies suggest that the quantity of βcells plays a crucial-role, in glucose-homeostasis Augusto et al[16]The reduction in β cell mass has been documented associated with the epigenetic suppression of the Pancreatic Homeobox Transcription… factor (Pdx1), which plays a crucial role in normal differentiation of βcells during embryonic development·Pnney et al[36]Moreover, prolactin plays a crucial role in promoting sufficient β-cell proliferation, as evidenced by studies involving mouse knockouts lacking the prolactin receptor(PrlR-/-) Auffret et al[9]
Gluco toxicity is occur due to the result of β cell apoptosis over time Ashcroft et aal[7]
Diminished β-cell hyperplasia is considered significant in gestational diabetes mellitus (GDM), supported by findings from animal research and limited post-mortem human studiesVan et al[47]

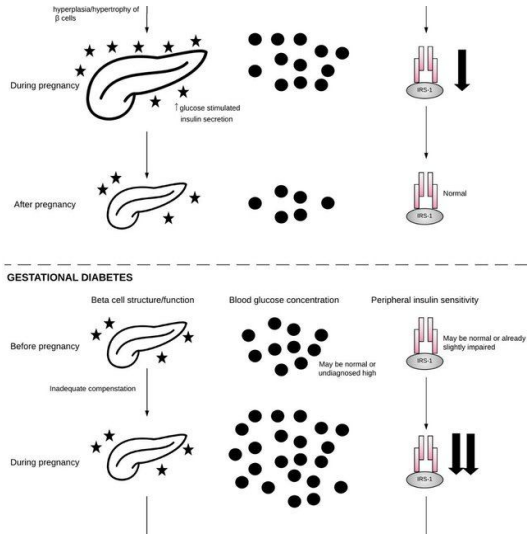


Fig. 1.1 β-cell dysfunction

Chronic insulin resistance in gestational diabetes mellitus (GDM) appears as a breakdown in insulin signaling,... leading to insufficient plasma membrane movement of glucose transporter 4 (GLUT-4) (Fig. 1.2). This results in a 54% reduction in insulin-stimulated glucose uptake compared to normal pregnancyCaatalanno& P.M[12]In gestational diabetes mellitus (GDM), insulin receptor abundance remains generally unaffected. However, altered tyrosine phosphorylation orincreases serine or threonine phosphorylation of insulin's receptor.. attenuates insulin's signaling pathways..Barbour et al[10]

Moreover,change in the movement and phosphorylation status of down stream middle people of insulin flagging, like insulin receptor substrate(IRS 1), phosphatidylinositol 3-kinase(PI3K), and glucose transporter-4(GLUT-4), have been observed in gestational diabetes mellitus (GDM)..Frieddman et al[20]

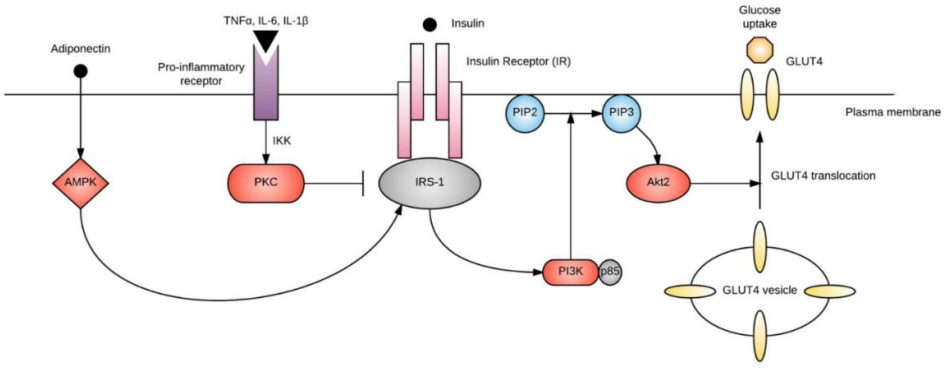


Fig. 1.2 In the insulin flagging pathway, insulin ties to the receptor IR, starting a fountain of occasions that manage glucose digestion. Upon insulin restricting, insulin receptor substrate-1(IRS-1) is actuated, prompts the initiation of phos phatidylinositol-3-kinase(PI3K). PI3K phosphorylatesphosphatidylinositol 4, 5 bisphosphates (PIP2) to shape phosphatidylinositol 3, 4, 5 phosphate (PIP-3), subsequently enacting... _

Akt2. Akt 2 advance the move glucose carrier 4(GLUT-4) to the cell film , works with the sugar take-up into the cells.

1.6. CURRENT TREATMENT PLANS FOR GDM

Insulin therapy:

Insulin is the preferred treatment for GDM ifDetermining insulin dosage during pregnancy for gestational diabetes mellitus (GDM) poses challenges due to fluctuating insulin sensitivity throughout pregnancy. Recommendations for insulin dosing are not specifically tailored for GDM, despite efforts to manage high blood sugar levels through diet and exercise modifications. Insulin requirements typically increase as pregnancy progresses, particularly in the later stages of the second or third trimester, reflecting heightened insulin resistance associated with advancing gestation[4]

Insulin resistance progressively rises during pregnancy, leading to an approximate total daily insulin requirement of 0.8-0.9 units per kilogram of body weight Gonzelez et al[22]

Oral medications:

When deciding the safe drug in pregnancy then Glyburide and Metformin are the only two drugs. The general Dosage protocols for glyburide and metformin in gestational diabetes mellitus (GDM) closely resemble those use in the management of type2 diabetes mellitus.

Consider, improved fetal outcomes, such as decrease incidence of Macrosomia (excessive birth weight) & Large for Gestational Age (LGA), observed in direct comparisonsbetween metformin and glyburide, along with increases incidence of neonatal hypoglycemia in glyburide studies, metformin may be considered a preferred optionKelley et al[29]

Glyburide and metformin are both available as genericmedications, offering cost advantages to patients compared to insulin therapy. They are administered one to two times daily, depends on the specific dosages and formulation chosen Kelley et al[29]

CHAPTER 2

LITERATURE REVIEW

2. LITERATURE REVIEW

Mustafa Abid *et al.*, (2024) Fabrication and in-vitro characterization of mucoadhesive tablet using a natural biocompatible polymer containing metformin HCl.
The study found that increasing mucoadhesive polymer in a tablet decreases its release rate. Release kinetics modeling, conducted through regression analysis, revealed sustained release patterns. Among all formulations, the results of F7 were excellent and met the standards required for sustained-release mucoadhesive formulation.

Pankti *et al.*, (2024)Drug-stacked veggie lover chewy candies for customizedhow to take simethicone: A plausibility investigation of semi-strong expulsion based on 3D printing of a low-calorie drug made from gelatin chewy candies.
3D-printed chewy candies are viewed as a creative dose structure where portion, size, shape, and flavor may be tweaked. Also, it lessens the requirement for molds and handling by experienced laborers.

Zimmerman C Scott *et al.*, (2023) Metformin End and Dementia Occurrence.
In this review, ending metformin therapyis related with expanded dementia occurrence. This might have significant ramifications for the clinical care of grown-ups with diabetes and gives extra proof of metformin is related with decreased dementia danger.

Dunne Fidelma *et al.*, (2023) Early Metformin in Gestational Diabetes. A Randomized Preliminary.
Early treatment with metformin was not better than fake treatment for the composite essential result. Prespecified optional result information support further examination of metformin in bigger clinical preliminaries.

Akram S. *et. Al.*, (2023) Audit on Pharmacological treatments for the administration of Gestational Diabetes.
Oral meds like glyburide and metformin are the most suggested first-line treatments, yet on the off chance that ideal glucose control isn't accomplished, analogs, for example, aspart, lispro, and detemir might be required. Patient assessment is significant to choosing the best treatment choice.

Kale Pratiksha *et al.*, (2023) Plan and Assessment of Home grown Palatable Chewy candies containing Ginger Powder to Treat Oral Thrush.
Ginger powder natural chewy candies were created and assessed for their capability to fix oral thrush. The making of novel natural measurement structures and the assessment of the effect of different home grown prescriptions on oral thrush were the significant explanations behind the interest in such a dose structure.

Benton *et al.*, (2023) The effect of Gestational Diabetes mellitus on saw mother-newborn child holding: A Subjective Report
It was found that GDM can adversely affect apparent mother-newborn child holding, which seems to change all through the perinatal period. Further observational exploration is expected to help with understanding the effect of GDM on mother-baby holding and the potential intervening impact of mental problems, including despondency.

Adel *et al.*, (2023) Metformin: proof from preclinical and clinical examinations for expected novel applications in cardiovascular sickness.
Metformin has a few conceivable expected components of cardiovascular advantage past its glycemic impacts remembering calming impacts and decreases for oxidative pressure, body weight, and pulse.
Metformin may likewise have helpful impacts in people without type2 diabetes.

Gupte S.*et al.*, (2023) Commonness and results of Gestational Diabetes mellitus in Indian Ladies: Experiences from an enormous true concentrate north of 10 years at the tertiary consideration research organization.
The information of 20,232 pregnant ladies from June 2012 to 2022 walk was recovered and investigated. Sum of 2192 women revealed GDM. A sum of 646 (29.47 percent), 1149 (52.42 percent), and 397 (18.11 percent) pregnant women were determined to haveGDM throughout the first, second, and third trimesters of pregnancy, individually. Neonatal inconveniences were examined, and 14 neonatal passings were noted. Likewise, checking and treatment of ladies with GGI assume a critical part in forestalling the movement of GGI to GDM.

Camargo *et al.*, (2023) New sources of Pectin: Extraction, processing, and Industrial uses.
New sources of pectin include the cladodes of Opuntia fiscus indica, Chayote, Pumpkin, and Eggplant.Due to their high production and physicochemical properties, citrus fruits and apples are the primary sources of pectin.. As alternatives to overexploited sources, organic by-products like hulls, husks, and seeds, from which pectin with specific physicochemical properties can be obtained for a variety of applications, have been sought in recent past.

Sabbagh *et al.*, (2022) Assurance of Metformin in fixed-portion mix tablets by ATR-FTIR spectroscopy.
The consequences of the model demonstrated great coherence with a relapse a coefficient of 0.9997 (R2). The square root of mean blunder of alignment, It was 0.447 (RMSEC). 3business FDC medications with 500 mg of metformin per tablet were evaluated.

Chen Sheng *et al.*, (2022)Metformin in endlessly maturing related sicknesses: Clinical applications and pertinent components.
Particular sub-atomic components through which metformin weakens maturing and different maturing related illnesses are still ineffectively perceived and still need to be explored exhaustively. A superior comprehension of these systems will extraordinarily work with the improvement of novel and effective procedures for the counteraction and treatment of endlessly maturing related sicknesses by metformin.

Maria J. *et. Al.*, (2021)Metformin for diabetes during pregnancy concentrate on A randomized trial comparing metformin and insulin in gestational diabetes, glycemic control, and obstetrical and perinatal outcomespreliminary.
The use of metformin was related with preferable after-dinner glycemic command over insulin for certain dinners, a lower chance of hypoglycemic episodes, less weight gain by the mother, & a low pace of disappointment as a separated therapy.

Meligi M. *et. al.*, (2021)Supported In vitro and In vivo conveyance of Metformin from Plant Dust Determined composite Microcapsules.
A flexible plant-dust determined defensive double microencapsulation stage for metformin (MTF), the first-line diabetes medicationwas produced for improved bioavailability.

Ozoude*et al.*, (2020) Detailing and improvement of the metformin-stacked microspheres utilizing Co-polymerization with Khaya senegalensis (Meliaceae) gum FTIR investigations showed no critical connection between unadulterated metformin hydrochloride with excipients. Mixes of sodium alginate and gum of Khaya senegalensis are promising polymersblends for the planning of controldischarge details. The mix of the khaya gum and sodium alginate created microspheres with properties for controlled discharge.

Sert Y. *et. al.*, (2020) Gestational Diabetes Screening and Conclusion.
screening and conclusion strategies for GDM acknowledged by various review gatherings will be talked about which will be trailed by the assessment of various glycemic limits.

Maheshwar M. *et al*., (2019) Impact of Temperature and Dampness on the Physical and Substance properties of Metformin Hydrochloride Tablets.
I reasoned that metformin hydrochloride tablets, when put away in an unseemly stockpiling condition that is generally in high stickiness, can cause speed increase changes in the physical and substance properties of the tablets, prompting a less compelling medication.

Panda k. *et. al.*,(2019) Application Capability of Gelatin in Medication Conveyance.

The gelatin properties can be improved and synthetically changed to shape composites, mixes for a variety of drug applications. It has been used possibly as a polymer for designated drug conveyance.

Gertin Kaja *et al.*, (2019) Improvement of vitamin D sticky enhancements and their time span of usability

The agar chewy candies in this study were more delicate and begun to break in week seven while the gelatin chewy candies didn't break by any means over the period when a similar power was utilized. Over the long haul, the agar chewy candies got less firm yet stickier while gelatin chewy candies got firmer and harder. Agar chewy candies were stickier than gelatin chewy candies which was additionally seen by the creator in week seven

Vipul *et al.*, (2018) Gelatin from Organic product strips and its purposes as Drug and Food grade: A Distinct survey.

Gelatin figures out jam, jams, dessert shops, saves, natural product juices, and a lot more items that can be handily shaped. On account of therapeutic items, it mostly fills in as a limiting specialist in tablets, it is likewise utilized as a seasoning specialist, shading specialist, covering specialist, and balancing out specialist. Gelatin is additionally valuable in the detailing of the shell of the container.

Santhosh *et al.*, (2018)Improvement and portrayal of Metformin stacked Gelatin Nanoparticles for T2 Diabetes Mellitus

The outcomes showed that the PCMNPs are haemo-viable and hence, ok for oral organization. The glucose take-up was expanded 1.5 overlap in RBCs and L6 skeleton muscle cell line contrasted and Metformin. Subsequently, the planned nanoparticle framework could be favorable concerning drawn out discharge, to accomplish decreased portion recurrence and work on persistent consistence.

Zhen M. *et. al.*, (2018)Longer term results in offsprings of GDM moms treated with Metformin versus Insulin.

The MiG TOFU investigation discovered that the posterity of metformin-treated moms had a slight however genuinely huge expansion in biceps skinfolds, mid-upper arm perimeters, and subscapular skin folds

Khin O. *et. al.*, (2018)Indicators of Metformin disappointment in Gestational Diabetes.

Metformin disappointment bunch at OGTT, had a higher HbA1c, maternal age, and fasting glucose level, and prior age of conceptionat drug commencement. Metformin disappointment was anticipated on the off chance that Level of OGTT at rest greater than 4.8 mmol/l (69% awareness and 62% particularity).

Irma Silva *et al.*, (2017)Maternal sustenance: Potential open doors in the anticipation of gestational Diabetes.

Grasping the expected advantages of joining explicit nourishing enhancements, as well as dietary and way of life counsel, and distinguishing responsive subpopulations address an extraordinary chance to foster systems that mean to break the cycle and decrease the weight of metabolic illness by lessening the gamble of GDM in populaces

Kristi W Kelley *et a*l., (2015) A survey of Current treatment techniques for gestational diabetes.
The adequacy and wellbeing of treatment modalities for GDM have been the wellspring of much discussion as of late, both glyburide and metformin are oral specialists currently suggested in numerous rules as a proper choice for overseeing patients with GDM.

Sayed *et al*., (2014)Detailing Advancement and Assessment of Metformin Biting gum with harsh taste concealing
The biting gum measurements content was around 86.2%. The delivery pace of metformin biting gum was around 70% after 5 min of rumination. Concealing the unpleasant taste of the medication was accomplished by utilizing acesulfame-isomalt as a sugar and setting it up with freeze-drying hardware.

Hamid N. *et al*., (2014)Nutraceuticals are items, other than nourishment that are additionally utilized as medication.
They function as restorative as well as dietary specialists. A nutraceutical item might be characterized as a substance, which has physiological advantage or gives security against constant sickness. Nutraceuticals help to further develop wellbeing and, defer the maturing system, forestall constant illnesses, increment future, or backing the design or capability of the body moreover.

Lautatzis*et. al*., (2013) Viability and wellbeing during pregnancy in Metformin, ladies with gestational diabetes mellitus or polycystic ovary disorder: An efficient survey.
Proof recommends that there are expected benefits for the utilization of metformin in GDM over insulin regarding weight gain in maternity and neonatal results. Besides, patients are more tolerating of metformin than insulin.

Ghanshyam Y. *et al*., (2013)These days numerous nations are searching for the utilization of home grown drugs because of their extremely less secondary effects and different characteristics as well. As natural medications have different pharmacological exercises and a large number of characteristics, they can be likewise utilized in various corrective arrangements. Regular polysaccharides are utilized in an enormous number of various arrangements and they are non-harmful likewise, they are utilized in various drug arrangements as well as in superficial arrangements

Srinivasan B. *et al.*, (2011)compound alteration is extremely fundamental and advantageous to improve the limiting property of the gelatin. The acetylation of the free hydroxyl bunches keeps an eye on the better return of gelatin and the acetylation should be possible effectively by utilizing acetyl chloride in ethanol at 20%, 40%, and 60% v/v and it prompts different Adjusted Gelatins.

Balani J. *et al.*, (2009)Pregnancy results in ladies with Gestational diabetes treated with Metformin or insulin: A case control study.
Ladies with metformin-treated GDM and with comparative gauge risk factors of unfriendly pregnancy results had low weight gain and further developed neonatal results contrasted andinsulin-treated patients.

CHAPTER 3

Aim & objective

3. AIM & OBJECTIVE

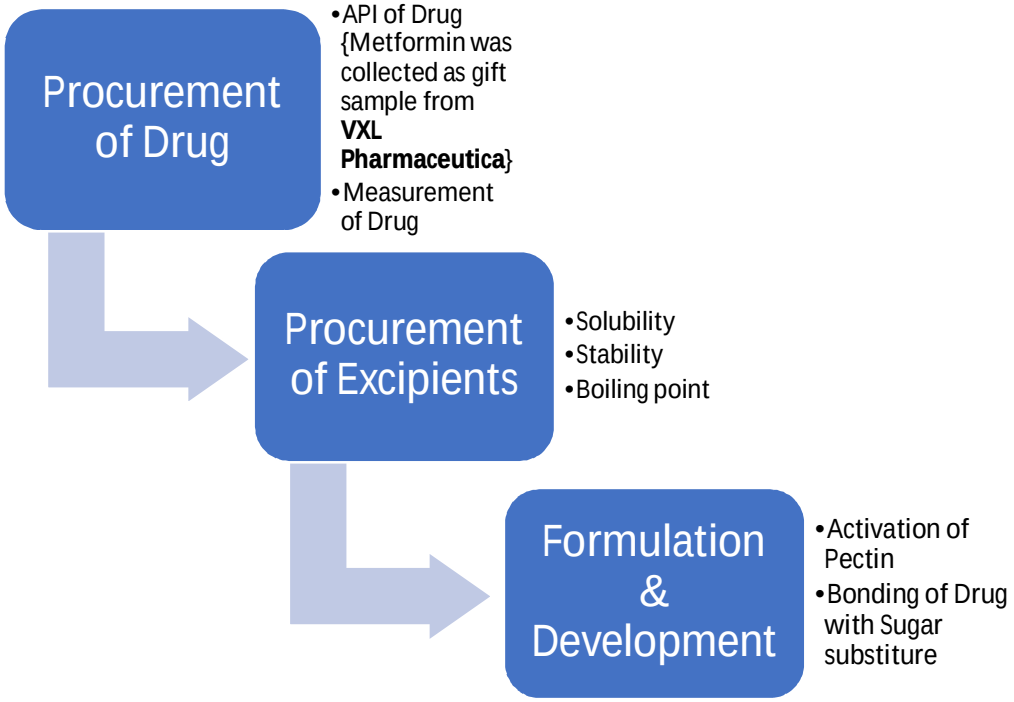
3.1 PLAN OF WORK (EXPERIMENTAL DESIGN)

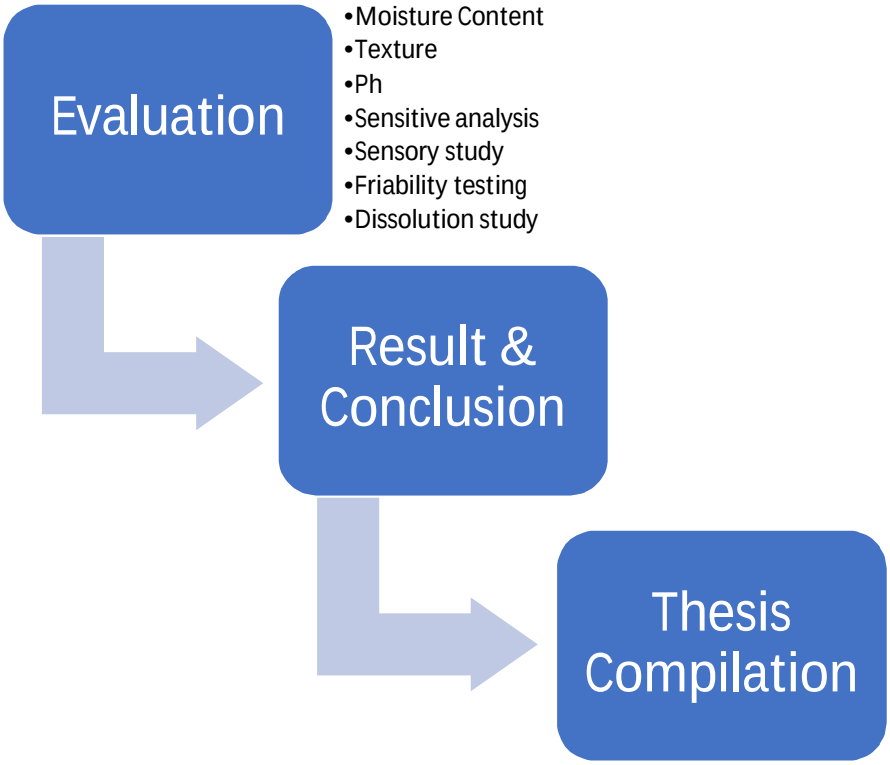
Keeping the objectives of the study in mind, the following plan of work followed

1. RESEARCH PHASE

Literature Review: Gather information on Gestational Diabetes, Metformin, Gummies, and excipients.

Formulation Design: Decide on the formulation strategy for gummies (e.g., techniques, excipients).





DATA ANALYSIS

Statistical Analysis: Analyze experimental data using appropriate statistical methods to conclude.

Interpretation: Interpret results in the context of the research objectives and existing literature.

DOCUMENTATION AND REPORTING

Thesis Writing: Compile findings, discussions, and conclusions into a cohesive thesis document.

Presentation: Prepare presentations summarizing the research for academic or professional audience.

3.2AIM & OBJECTIVE

Aim:

The primary aim of this thesis is to develop a novel formulation of vegan gummies containing Metformin for the management of gestational diabetes. Through a comprehensive research approach, the aim is to investigate the feasibility of incorporating metformin into a gummy formulation that is both effective and acceptable for pregnant women following a vegan lifestyle.

Objectives:

I. Develop a formulation for Metformin vegan gummies suitable for pregnant women with gestational diabetes, adhering to a vegan diet lifestyle.
II. These gummies aim to offer a plant-based alternative.
III. It will offer a convenient dosage form in the form of gummies, which are easy to consume and carry.
IV. Enhance compliance with the medication regimen by providing a palatable and enjoyable option for medication administration, thereby promoting adherence to treatment protocol.
V. Ensure that the gummies maintain the safety and efficacy profile of traditional metformin medications while meeting the specific needs and preferences of pregnant individuals following a vegan lifestyle.
VI. The main objective is to offer well-tolerated, convenient, and effective options for managing gestational diabetes, ultimately improving maternal and fetal health outcomes during pregnancy.

CHAPTER 4

DRUG & EXCIPIENTS

4.1 DRUG PROFILE

Drug name: Metformin

Metformin is a very known medication prescribed for the treatment of Diabetes Mellitus. It belongs to the biguanides class of drugs and is considered the 1st-line medication for the treatment of type2 diabetes mellitus.

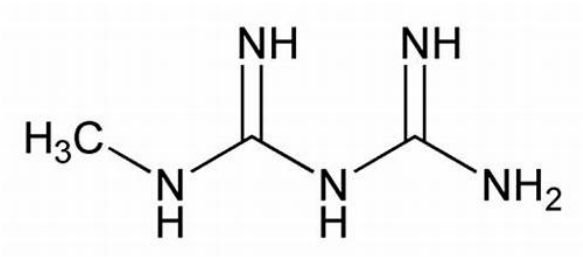


Fig. 4.1: Structure of Metformin

- Formula: C4H12N4
- Chemical Name: N, N dimethyl li mid o dicarbon imidic diamide
- IUPAC Name: 3-(diamino methylidene)-1,1-dimethylguanidine
- Molar Mass: 129.16
- Melting Point: 223-226°C
- Boiling Point: 224.1°C at 760 mm Hg
- Description: White, Hygro_scopic- Powder characterized by a bitter taste.
- - Solubility: It dissolves well in water and shows slight solubility in alcohol.
- and Partially insoluble in- ether, chloroform, acetone, methylene chloride.
- Vapor Pressure: 1.3± 0.3 mm Hg at 25 °C
- Half-life: 6.2 hours in the plasma, 17.6 in blood.
- Log P- -2.6
- Decomposition: Upon decomposition by heat, it releases toxic fumes containing nitric oxide.
- PH- 2.7
- pKa- 2.4

Metformin functions as an antihyperglycemic agent rather than a hypoglycemic one. It operates independently of insulin secretion from pancreatic β-cells and does not induce hypoglycemia, even at higher doses Hardman et al[24]Metformin primarily reduces glucose levels by inhibiting hepatic gluconeogenesis and enhancing peripheral insulin insensitivity in muscle and adipose tissues.

Absorption, Distribution, and Excretion:

It is ingested orally. Metformin is absorbed slowly and incompletely from the gastrointestinal tract, primarily from the small intestine. The absolute bioavailability of a 500 mg dose of Metformin when administered in the fasting state ranges between 50% to 60%. Steadystate plasma conc. of Metformin are regularly

accomplished inside 24 to 48hours and are ordinarily estimated at focuses below micrograms per milliliter (<μg/mL).
It is substantially excreted by the Kidneys. Renal tubular secretion is the major route of metformin excretion[5]

Metabolism:
Metformin undergoes no hepatic or gastrointestinal metabolism and is not excreted in bile. No metabolites of Metformin have been detected in humans.[6]

Mechanism of action:
Metformin exerts its antihyperglycemic effects through several mechanisms: it reduces hepatic'sglucose creation, restrains gastrointestinal glucose retention/, and improves fringe glucose' take-up and usage by expanding insulin responsiveness.

Dosage & Administration:

- For adults with type 2 diabetes, the usual starting dose is typically 500 mg or 850 mg once or twice daily with meals.
- Dosage may be gradually increased based on blood glucose levels and tolerability, with a maximum recommended dose of 2000-2500 mg per day.
- Extended-release formulations are usually taken once daily with the evening meal.
- Dosage adjustments may be necessary in patients with renal impairment to prevent the risk of lactic acidosis.

Side effects:
Common side effect's of metformin include:

- Gastrointestinal disturbances such as - diarrhea, nausea, vomiting, and abdominal' discomfort.
- Metallic taste in the mouth.
- Headache.
- Hypoglycemia (when used in combination with other antidiabetic agents).
- Rarely, lactic acidosis (especially in patients with renal impairment or other predisposing factors).

Precautions & Warnings:

- Metformin should be used with caution's in patient's with impaired renal functions, as it can accumulate in the body and increasethe gamble of lactic acidosis.
- It is contraindicatesin patients with extreme renal disabilities (eGFR<30 mL/min/1.73 m^2)/or conditions predisposing to tissue hypoxia (e.g., severe respiratory disease, shock, sepsis).

- Metformin should be temporarily discontinued before radiographic studies involving intravascular iodinated contrast agents and restarted only after renal function is confirmed to be normal.
- Alcohol consumption should be limited while taking metformin due to the increased risk of lactic acidosis.

Drug Communications:

- Metformin mayinterface with specific drugs, including cimetidine, carbonic anhydrase inhibitors, corticosteroids, diuretics, and drugs that affect renal function.
- It may potentiate the hypoglycemic effects of insulin and sulfonylureas, necessitating dosage adjustments.

4.2 EXCIPIENTS PROFILE

Pectin:

Pectin is a versatile polysaccharide with diverse applications in the food industry, cosmetics, pharmaceuticals, and biomedicines. It is used as a thickener, gelling agent, and stabilizer. In pharmaceutical formulations, pectin may serve as a binder, disintegrant, or controlled-release agent in tablets and capsules. It is also utilized in oral suspensions and gels for drug delivery.

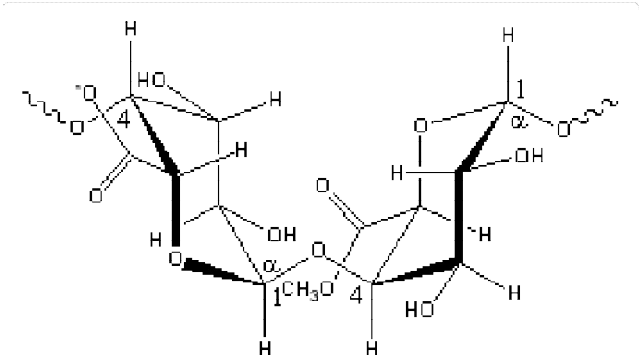


Fig. 4.2 Structure of Pectin

Chemical Structure and Properties: Pectin is a complex heteropolysaccharide composed mainly of long chains of α 1,4 connected D-galacturonic.. corrosive units. These chains may be interspersed with regions containingunbiased sugars like D-galactose, L-arabinose, and D-xylose. The level of esterification (the degree to which the carboxyl gatheringsare esterified with methanol) and the molecular weight of pectin can vary, influencing its functional properties.

Safety and Regulations: Pectinis by and large perceived as protected (GRAS) by administrative specialists like the U.S. Food and Medication Organization (FDA) and the European Food handling Authority (EFSA)., when used per good manufacturing practices. However, individuals with allergies to fruits or certain plant-derived substances should exercise caution, as allergic reactions to pectin have been reported in rare cases.

Xylitol:

It helps to reduce the risk of cavities.

It has anti-aging properties and inhibits bacteria growth.

Sorbitol:

It is used as a sugar substitute that tastes sweet but has no calories.

It acts as a humectant.

Citric Acid:

It is a water-soluble ingredient that pulls the moisture out of the gummies and makes them melt. It acts as a preservative.

Isomalt:
It has sugar-like physical properties.
It will be used with Metformin to mask the bitter taste of the drug.

Flavoring agent:
Cinnamon powder

Coloring agent:
Safranin for red color.

CHAPTER 5

MATERIALS & METHODOLOGY

5.1 PRE-FORMULATION PARAMETERS

5.1.1 Solubility Studies: By solubility studies, it was found that Metformin is high solublilityin water, restricted dissolvable in liquor, and insoluble in CH3)2CO and methylene chloride.

5.1.2 Organoleptic properties: In organoleptic studies of Metformin, the color was found to be white, taste was bitter. Under the microscopic examination, Metformin was found to be crystalline powder.

5.1.3 Identification by FTIR: Utilizing IR, the drug was examined. It was possible to get spectra of metformin. Triturates about 1milig of the test sample with, approx. 300mg of finely powdered, potassium-bromide (previously dried at 105℃ for 2 hoursFirst, thoroughly grind the mixture and uniformly distribute it in reasonable die. Then, pack it under vacuum' conditions at a tension approximately equal to 8 hundreds megapascals (MPa).

Place the resulting disc into an appropriate holder within the spectrophotometer.

Place the pellet in the pellet holder in the spectrophotometer. Then, Record the spectra in the range of 2.60µm-15µm of the test sample and the standard Metformin hydrochloride.

5.1.4 Identification by Chemical: When a chemical silver nitrate test solution is applied to solutions containing chlorides, it results in the formation of awhite' curdy ppt. This encourage is insoluble in the nitric corrosive, but can be dissolved in a slight overabundance of 6 N ammonium hydroxide.

5.1.5 Loss on Drying: Take a LOD bottle with a stopper (previously dried at 105°C for 30 minutes). Let its weight be W_1. Place about 1g of test sample in the dried LOD bottle, replace the stopper, and accurately weigh the bottle with its contents. Let its weight be W_2. Uniformly distribute the contents in the bottle by gentle side-wise shaking.Place the stacked jugs in the stove, eliminate the plug, and leave it in the broiler chamber to dry at 105°C±2 for 5 hours. In the wake of drying, eliminate the container with the plug still in its place and permit to cool in the desiccator prior to gauging.

5.1.6 Assay by HPLC:

Cradle: 9.8 g/L of monobasic ammonium phosphate' in water.

Versatile stage': Cradle and acetonitrile (95:5). Change by phosphoric corrosive to a pH of 3.0.

Standard Arrangement': 0.05 mg/ml of USP Metformin hydrochloride R S in the versatile stage. Sonication can be utilized to advance' disintegration. Permit the answer for equilibrate to surrounding temperature.

Test Arrangement': 0.05 mg/ml of metformin hydrochloride in versatile - stage. Sonication can be utilized to advance disintegration.Allow the solution to equilibrate to ambient temperature.

Chromatographic System
Mode: LC
Detector: UV at 215 nm
Segment: 4.6 mm x 25 cm; 10 µm pressing L9
Stream rate: 1.5 mL/min
Infusion volume: 20 µL

Framework reasonableness:
Test: Standard arrangement
Reasonableness standards:
- Following component: Limit of 2
- Relative standard deviation: Limit of 0.73%
Investigation
Tests: Standard arrangement and test arrangement.

5.2 MEASUREMENT OF METFORMIN

The recommended dose range for achieving glucose-lowering efficacy with Metformin typically falls between 500 to 2000 mg each day. Dose ought to be customized for every patient based on considerations of both the effectiveness and the tolerance, while ensuring it does not surpass the maximum daily limits recommended, which are2550 mg for grown-ups and 2000 mg for pediatric patients matured more than 10 years old.

Table 5.1 Portion estimation of Metformin

		Starting Portion	**Titration Portion**	**Max.Portion**
Grown-ups	Quick - discharge Metformin	500-850 mg day to day	500-850 mg weekly	2550 mg in a day
	Extended-release Metformin	500-1000 mg daily	500 mg week by week/in about fourteen days	2000 mg in a day
Pediatrics	Immediate release Metformin	500 mg day to day	500 mg in a week	2000 mg day to day
	Expanded discharge Metformin	-	-	-

Each gummy contains 250mg of Metformin. Every dose of metformin is added to the wet gelatin combination when the blend temperature is below 65°C by measured quantity.

5.3 FORMULATION OF VEGAN GUMMIES

Step 1: Dry-Mix Pectin

Pectin should be dry mixed with the first measurement of xylitol and sorbitol in this preparation.

Doing this will prevent clumps as the pectin can be more evenly distributed.

Step 2: Hydrate Pectin Mixture

Mix the sugar substitutes and pectin with the first measurement of water once this is combined and free of any clumps.

Add it to the second measurements of sorbitol and xylitol.

Place the entire mixture into the beaker and place it on a heating mantle over medium heat.

Gently heat the mixture until it comes to a simmer.

Monitor the temperature witha thermometer.

Continue to heat this mixture to 250°F. This temperature is higher because the sugar substitutes need slightly higher temperatures to get the same texture.

Fig. 5.1 Hydration of Pectin

Step 3: Flavoring and Coloring

Add cinnamon powder for flavor and Safranin for red color.

Vigorously whisk the mixture to ensure even color and flavor.

The sugar substitutes will not crystallize as table sugar does.

Fig.5.2 & 5.3 Addition of flavor & color respectively

Step 4: Add Metformin

Mix the Metformin with isomalt manually.
Directly mix this mixture with the pectin base at the temp. below 65°C.

Step 5: Prepare Citric Acid Solution
A 3:1 ratio of water to Citric acid is preferable.
Use a dropper to add anywhere from 1 ml to 2 ml of the solution to the mold, depending on the size of the gummies.

Step 6: Pour into molds
Once the mixture has been added to the molds, Spray the top with more of the acidic solution. This will help speed up the gelling process.
After about two hours the gummies can be removed from the molds and set to dry at room temp.
Spray them with another round of the acidic solution before drying.
Over time the acid will slowly penetrate through the entire gummy and set it.

Fig. 5.4 Prepared gummies

5.4 EVALUATION PARAMETERS

1. **PH of the gummy**

   To measure the pH of the jelly, a digital pH meter is employed.

   A sample of 0.5 g from the pre-weighed formulation is dispersed in 50 ml of water, and the resulting pH is recorded. The gummies are blended to form a uniform paste.

   The pH meter is calibrated and the example temperature is acclimated to room temperature before pH estimation.

   The PHelectrode is rinsed with distilled water and immersed in the gummy paste to measure the pH accurately.

2. **Texture profile analysis**

   Hardness: Hardness is determined usinga pressure test utilizing a huge ball indenter, mimicking the crushing of sticky items among thumb and index finger. This test establishes upper and lower tolerance limits for the product based on hardness parameters.

   Softness: Softness, in contrast to stiffness, which is measured by bending length, is characterized as the opposite of firmness or hardness, assessed through consistency tests. It reflects the tactile perception of the gummy product's pliability and resilience.

3. **Dissolution study**

   Warm the disintegration medium i.e., water to 36.5 ° to 37.5 °. Place one sticky in the device, covering the vessel, and work the contraption at the predetermined rate. Following 2 active times in the corrosive medium, pull out an aliquot of the fluid and speed incontinently as coordinated under the Cradle stage.

4. **Sensory Evaluation**

   The sensory evaluation parameters include hardness, cohesiveness, gumminess, andchewiness.

5. **Moisture Substance**

   The dampness content of the gummies was assessed according to ISO 6496-1999 guidelines. Gummies were prepared by cutting them into small pieces and approximately 5 grams of each sample were weighed into dried ceramic containers, which were previously dried and weighed. The samples were subjected to drying in a broiler kept up with at 103°C ± 2°C for a time of 4 hours. In the wake of drying, the examples were cooled in a desiccator to keep dampness reabsorption from the climate. In this manner, the examples were re-weighed to decide the dampness content.

6. Content Uniformity test

Individually weighed 10 gummies and crushed in the mortar & pestle. Place the crushed gummy powder into a volumetric flagon and add a known vol. of solvent (mixture of 100 mL of distilled water & methanol).

Sonicate the solution for 30min to enhance dissolution. Filter the solution and collect the supernatant part.

For HPLC,

i) Prepare a progression of metformin standard arrangements of known concentrations to create a calibration curve.
ii) Inject these standards into the HPLC system to obtain their respective peak areas.
iii) Inject the sifted test arrangements into the HPLC framework.
iv) Record the retention time and peak area for metformin in each sample.
v) Plot the peak areas of the standard solutions against their concentrations to create a calibration curve.
vi) Use this curve to determine the concentration of metformin in each gummy sample.

5.5 IN-VITRO DRUG RELEASE STUDY

Comparison of dissolution rate of Metformin hydrochloride tablet and Metformin Gummy. Gummies as per the result show controlled release of drug for prolonged action. Metformin on the other side shows immediate release.

Dissolution Testing Steps:

I. Preparation of Dissolution Medium: The dissolution medium, often a buffer solution such as 0.1N HCl/ phosphate buffer (pH 6.8), is prepared and; maintained at 37°C ± 0.5°C to simulate physiological conditions.
II. Placement of Dosage Form: The dosage form (gummy or tablet) is placed in the dissolution vessel.
III. Agitation: The paddle is set to rotate at a specified speed (e.g., 50 rpm for gummies and 75 rpm for tablets).
IV. Sampling: At predetermined time intervals(e.g., 5, 10, 15, 30, 45, an hour), samples of the dissolution medium are 5mL withdrawn using the pipette and replaced with fresh medium to maintain a constant volume.
V. Analysis: The samples are analyzed using UV HPLC to determine the concentration of metformin released.

Dissolution Mechanism Metformin Gummies:

Matrix System: Pectin acts as a hydrophilic matrix in the gummy formulation. When the gummy comes into contact with gastrointestinal liquids, the gelatin expands, shaping a gel-like layer that controls the diffusion of metformin out of the gummy.

Controlled Release: The controlled release is achieved through the gradual disintegration of the gelatin lattice and the dispersion of metformin molecules through the hydrated layer.

CHAPTER 6

RESULTS AND DISCUSSIONS

6. RESULTS AND DISCUSSIONS.

6.1 PRE-FORMULATION PARAMETERS.

Identification by FTIR:

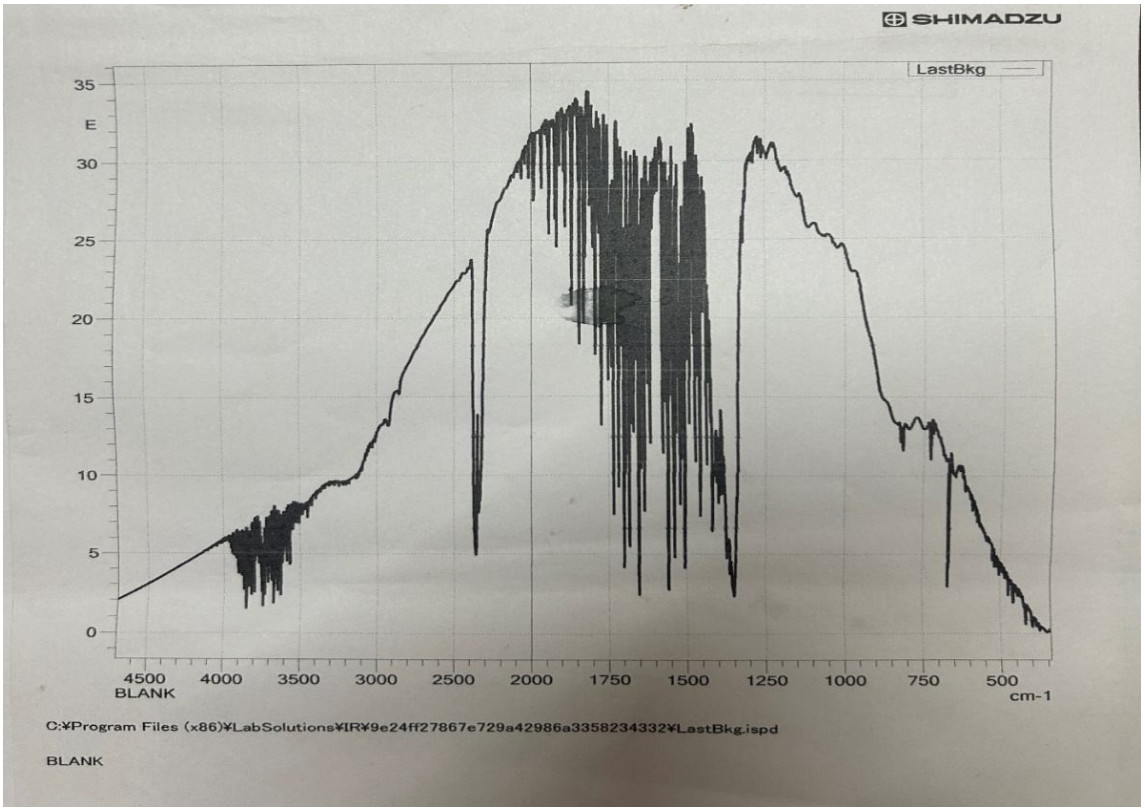


Fig. 6.1 Blank FTIR

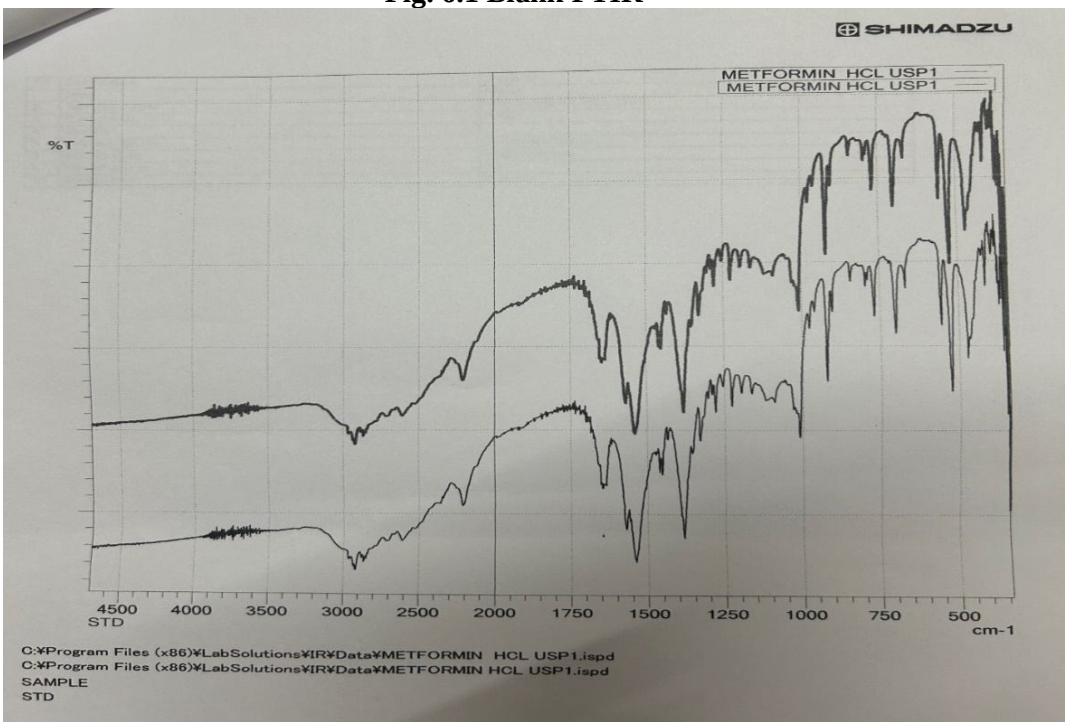


Fig. 6.2 FTIR of Metformin

Metformin exhibits specific vibrational modes in its molecular structure, characterized by functional groups such as imines (C=N−H), primary, secondary, and tertiary amines. Primary amines manifest two distinct NH bands in the range of 3500–3200 cm^{-1}, attributed to symmetric and asymmetric NH stretching. Secondary amines, however, display a single NH stretching band around 3100 cm^{-1}.

Infrared spectroscopy analysis reveals that the NH stretching modes (ν1-ν5) contribute significantly to the Polarization-Enhanced Direct detection (PED), with ν1 and ν3 specifically linked to asymmetric and symmetric NH stretching of the primary amine group in metformin. The NH stretching mode of the secondary amine is observed at approximately 3270 cm^{-1}, with ν1 and ν5 modes showing complete PED contributions to the imine group.

Furthermore, metformin's molecular structure includes C=N stretching modes observed at 1631 cm^{-1}, characteristic of the guanidine moiety. Guanidines typically exhibit strong absorption due to C=N stretching between 1600 and 1510 cm^{-1} in infrared spectra.

Assay by HPLC:

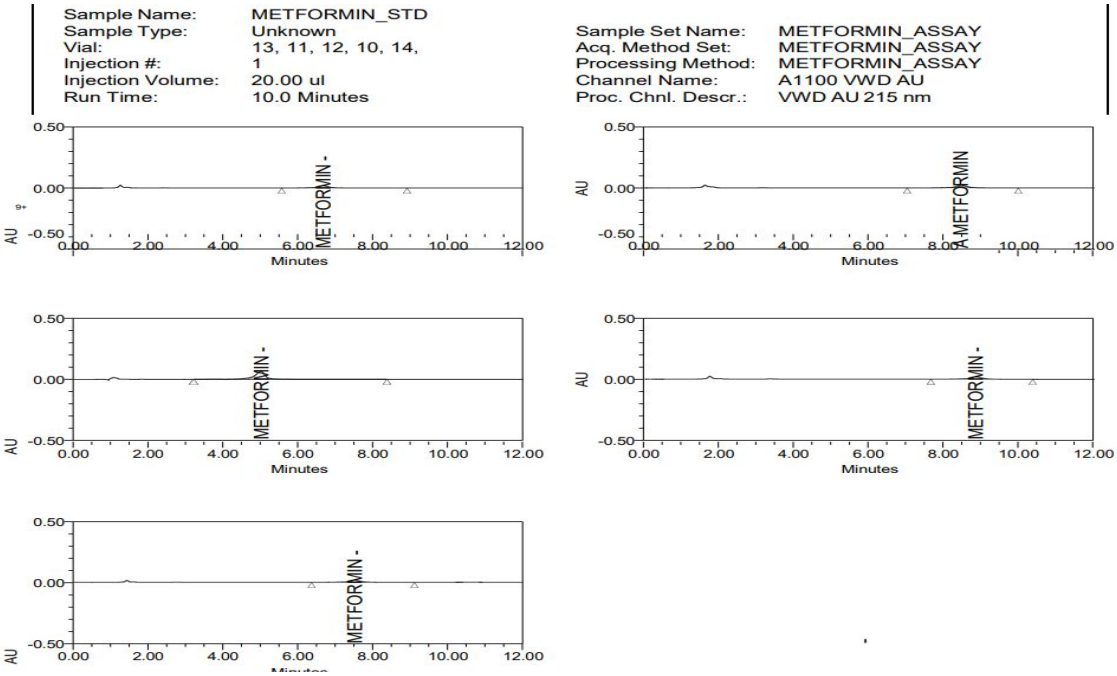


Fig. 6.3 HPLC of Standard Metformin

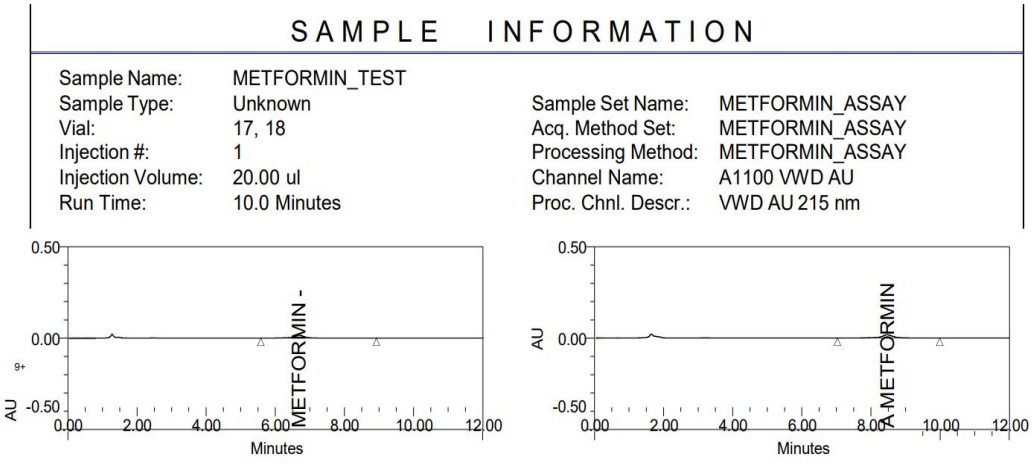


Fig. 6.4 HPLC of Test Metformin

Loss on Drying:

Wt. of LOD bottle (W_1)= 36.8791gm

Wt. of LOD bottle + Test sample (W_2)= 37.8871gm

Wt. of LOD bottle + Test sample after drying (W_3)= 87.8571gm

LOD= $\frac{W2-W3}{W2-W1} \times 100$ $= \frac{37.8871-87.8571}{37.8871-36.8791} \times 100$ = 2.976 %w/w

6.2 METFORMIN VEGAN GUMMIES CHARACTERISTICS

Table. 6.1 Characteries of Vegan Metformin Gummies

Characteristics	Description
Taste	Cinnamon & Sweet
Texture	Chewy but firm
PH	Neutral to slightly acidic
Viscosity	Consistent
Temperature stability	Require cool storage to prevent from melting due to high temperature
Humid stability	Resistant to moderate humidity; should prevent from moisture
Dosage	500mg of metformin per gummy
Release Profile	Designed for sustained or controlled release of metformin
Bioavailability	More gradual absorption due to the controlled release properties of the pectin matrix

6.3 EVALUATION PARAMETERS

Moisture Content % of gummies: $\frac{W2-W3}{W2-W1} \times 100$

Where:

Suppose the weights are as follows:

W1(Weight of the empty dish) = 50.00 g

W2(Weight of the dish + gummies before dry) = 80.00 g

W3(Weight of the dish + gummies after dry) = 65.00 g

Moisture Content (%)= $\frac{80g-65g}{80g-50g} \times 100$

Moisture Content (%)=$\frac{15}{30} \times 100$

Moisture Content (%)=0.5×100

Moisture Content (%)=50%

Therefore, the moisture content of the pectin-based vegan gummies is 50%.

Content Uniformity of Gummies:

Table. 6.2 Data of 10 gummies

Metformin Gummy	Weight (g)	Peak Area	Concentration (mg/mL)	Content (mg)
1	2	1250	2.50	250
2	2.1	1260	2.52	252
3	1.9	1240	2.48	248
4	2	1255	2.51	151
5	2.1	1270	2.54	254
6	2	1250	2.50	250

7	2.2	1275	2.55	255
8	2	1260	2.52	252
9	1.9	1240	2.48	248
10	2	1255	2.51	251

Mean content= $\frac{100+102+99+101+103+100+104+102+99+101}{10}$ = 101mg

Standard deviation= $\frac{\sqrt{(250-251)^2+(252-251)^2+(248-251)^2+(251-251)^2+(254-251)^2}}{10-1} \approx$ 2.28mg

Relative Standard deviation(%) = $\left(\frac{2.28}{251}\right) \times 100 \approx 0.91\%$

Interpretation of Result:

According to pharmacopeial standards (USP), the content uniformity criterion typically requires that the RSD should not exceed 6% for active ingredients in solid dosage forms.

An RSD of 0.91% indicates excellent uniformity.

6.4 IN VITRO DRUG RELEASE STUDY

$$\frac{\text{Test absorbance}}{\text{Standard absorbance}} \times \frac{\text{Concentration of Standard}}{\text{Concentration of Test}} 100$$

Table. 6.3. Drug release study of Metformin Tablet

Test 1		**279234**	**50**	**5**	**100**	**100**
		282564	100	50	5	
Result	98.82137					
Test 2		278247	50	5	100	100
		282564	100	50	5	
Result	98.47207					

Where,Test Absorbance=279234 and 278247

Standard Absorbance=282564

Standard weight=50mg

Table. 6.4 Drug Release study of Metformin gummies

In 5 min.		0.05	50	5	100	100
		0.45	100	50	51	
Result:	**11.111**					
In 10 min.		0.095	50	5	100	100
		0.45	100	50	5	
Result:	**21.111**					
In		0.138	50	5	100	100

15min.						
		0.45	100	50	5	
Result:	**30.667**					
In 30 min.		0.2	50	5	100	100
		0.45	100	50	5	
Result:	**44.444**					
In 45 min.		0.324	50	5	100	100
		0.45	100	50	5	
Result:	**72**					
In 60 min.		0.4	50	5	100	100
		0.45	100	50	51	
Result:	**88.889**					

Where, Test Absorbance=0.05,0.095,0.138,0.200,0.324,0.400
Standard Absorbance=0.450
Standard weight=50mg

6.5 Stability studies results

Storage Conditions:
Room temperature (25°C, 60% RH)
Refrigerated conditions (4°C, 45% RH)
Sped up conditions (40°C, 75% RH)

Sampling Intervals:
Initial (0 days), 1 week, 15 days, 20 days, and 30 days.

Table 6.5 Stability data of Metformin gummies

Parameter	Initial	1 week	15 days	20 days	30 days
Room temp. (25°C, 60%RH)					
Appearance	Clear	Clear	Clear	Slightly sticky	Slightly sticky
Weight variation (g)	2.5±0.1	2.5±0.1	2.5±0.1	2.4±0.1	2.4±0.2
Metformin content (%)	100	99.5	98	97	96
Ph	5.5	5.5	5.5	5.4	5.4
TVC (CFU/g)	<10	<10	<10	<10	<10
Refrigerated (4°C, 45%RH)					
Appearance	Clear	Clear	Clear	Clear	Clear
Weight variation (g)	2.5±0.1	2.5±0.1	2.5±0.1	2.5±0.1	2.5±0.1
Metformin content (%)	100	99	99.8	99.6	98

Ph	5.5	5.5	5.5	5.5	5.5
TVC (CFU/g)	<10	<10	<10	<10	<10
Accelerated (40°C, 75%RH)					
Appearance	Clear	Slightly sticky	Sticky	Sticky	Very sticky
Weight variation (g)	2.5±0.1	2.4±0.1	2.4±0.2	2.3±0.2	2.2±0.3
Metformin content (%)	100	97	95	93	90
Ph	5.5	5.4	5.3	5.3	5
TVC (CFU/g)	<10	<10	<10	<10	<10

Discussion

The stability data suggest that:

Room Temperature: Metformin gummies showed slight changes in physical appearance and minor degradation in metformin content over 30 days.

Refrigerated Conditions: Gummies remained stable with minimal changes in all parameters over 30 days.

Accelerated Conditions: Significant degradation in physical and chemical properties was observed, indicating that high temperatures and humidity affect the stability of the gummies adversely.

Conclusion

Metformin gummies made of pectin are stable under refrigerated conditions for up to 30 days. At room temperature, they show acceptable stability for up to 20 days. Accelerated conditions demonstrate the need for proper storage to maintain the quality and efficacy of the gummies.

6.6 SUGGESTION FOR FUTURE RESEARCH

Here are sone important points that should be discussed in future research for the formulation of Vegan Metformin gummies:

Incorporation of Additional Nutrients: Consider adding essential vitamins and minerals beneficial for pregnant women to create a more comprehensive therapeutic gummy.

Mathematical Modeling: Apply mathematical models to describe the release mechanism and predict the behavior of the drug release under various conditions.

Comparative Bioavailability Studies: Compare the bioavailability of metformin from gummies with that of conventional tablets.

Pharmacokinetic Studies: Lead in vivo examinations in creature models to survey the pharmacokinetic profile of the gummies.

Toxicological Evaluation: Perform toxicological studies to ensure the safety of the pectin-metformin combination, particularly focusing on maternal and fetal safety.

Design and conduct clinical trials to evaluate the efficacy, safety, and patient compliance of the pectin-based metformin gummies in pregnant women with gestational diabetes.

Regulatory Pathway: Study the regulatory requirements for approval of gummy formulations for use in gestational diabetes.

Advanced Manufacturing Techniques: Investigate advanced manufacturing techniques such as 3D printing or microencapsulation to improve the precision and consistency of gummy formulations.

CHAPTER7

CONCLUSION

7. CONCLUSION

The formulation and evaluation of pectin-based metformin gummies for gestational diabetes (GDM) represent a significant advancement in the therapeutic management of this condition. This study aimed to develop an alternative dosage form that enhances patient compliance, ensures effective drug delivery, and maintains therapeutic efficacy. The following key conclusions can be drawn from this research-

Formulation Success: The research successfully formulated metformin-loaded pectin gummies that were both palatable and stable. The use of pectin as a gelling agent provided an appropriate matrix for the sustained release of metformin, making it suitable for managingblood glucose levels in pregnant ladies with GDM.

Characterization and Stability: The formulated gummies were characterized for their physicochemical properties, including texture, taste, and stability. These parameters were optimized to ensure the gummies were not only effective but also appealing to the target demographic. Stability studies indicated that the gummies retained their integrity and drug release profile over the intended shelf life.

Controlled Drug Release: The pectin matrix facilitated a controlled release of metformin, which is crucial for maintaining steady blood glucose levels and reducing the risk of hypoglycemia. This controlled release mechanism was thoroughly evaluated through in vitro dissolution studies, confirming the gummies' potential for sustained therapeutic effects.

Enhanced Patient Compliance: One of the significant outcomes of this study is the potential for enhanced patient compliance. Traditional oral tablets can be challenging for some patients to ingest, particularly during pregnancy, due to nausea and vomiting. The gummy formulation offers a more palatable and convenient alternative, which can improve adherence to the prescribed treatment regimen.

Safety and Biocompatibility: The study also underscored the biocompatibility of pectin, a natural polysaccharide, which is non-toxic and safe for consumption during pregnancy. This is a crucial consideration in the formulation of any medication intended for pregnant women.

Future Directions: The promising results of this study pave the way for further research, including clinical preliminaries to affirm the adequacy and security of metformin gummies in a larger cohort of pregnant women with GDM. Additionally, exploring the incorporation of other therapeutic agents into similar gummy formulations could expand the scope of this novel drug deliver.

CHAPTER 8

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PUBLICATIONS

S.N.	Topic Name	Journal Name	Status
1	Exploring the synergetic potential of Metformin with Pectin for formulation of gummies to treat gestational diabetes: A review based on current evidences and Future directions	IJCRT	Published
2	Formulation and Evaluation of Metformin Vegan Gummies for Gestational Diabetes	CIS (Bentham) Impact factor: 3.4	Under communication

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Exploring The Synergetic Potential Of Metformin With Pectin For Formulation Of Gummies To Treat Gestational Diabetes: A Review Based On Current Evidence And Future Directions

-Shivangi, Dr. Garima Gupta, Ms. Saloni Manglik

Abstract:

Metformin is a widely used type-2 Antidiabetic drug that also helps in reducing the occurrence and risk of various Metabolic Disorders. Pectin is a Plant-based soluble dietary fiber. Both Pectin and Metformin have a role in glycemic control and their potential as an adjunct therapy in Diabetes management. This review includes the existing literature on combined use of Metformin and pectin, their synergetic effects and therapeutic implications, Potential benefits and challenges, Using Metformin and Pectin for Moms-to-Be, Impact of High-Temperature Exposure on Metformin-Pectin Interaction, Anti-Diabetic Flavors with Pectin, Future direction and Conclusion.

Keywords: Metformin, Pectin, Heat, Flavor.

Introduction:

Gestational Diabetes Mellitus causes risk to both mother and infant, highlighting the urgent need for effective therapeutic intervention. Metformin is a First-line pharmacological agent that is used in the management of Type-2 Diabetes mellitus and GDM due to its favorable safety profile and potential benefits for maternal and neonatal outcomes. On the Other hand, Pectin which is a soluble dietary fiber sourced from Plants, has gained attention due to its diverse health-promoting properties. Combining metformin with pectin may offer synergistic effects, enhancing the therapeutic efficacy while minimizing adverse effects associated with metformin monotherapy.

Metformin-Pectin Combination in Gestational Diabetes-

Gestational diabetes presents unique challenges in its management, necessitating careful consideration of treatment options to optimize maternal and fetal health outcomes. Metformin, through its mechanisms of action involving hepatic glucose production inhibition and improved insulin sensitivity, has demonstrated efficacy in controlling blood glucose levels during pregnancy. Pectin complements these actions by attenuating postprandial glycemic excursions, thereby contributing to overall glycemic control. Several studies have explored the synergistic potential of metformin with pectin in GDM management, reporting improved glycemic parameters and reduced insulin requirements compared to metformin alone. Furthermore, pectin's ability to modulate gut microbiota composition may confer additional metabolic benefits, making it a valuable adjunctive therapy in the management of GDM.

Mechanism of Action-

Metformin shows antidiabetic effects by inhibiting hepatic glucose production, enhancing insulin sensitivity in peripheral tissues, and reducing intestinal glucose levels. On the other hand, Pectin forms a viscous gel in the gastrointestinal tract, slowing down carbohydrate absorption and digestion, thereby attenuating postprandial glucose excursions. Pectin fermentation by gut microbiota produces short-chain fatty acids, which contribute to improved insulin sensitivity and glucose metabolism.

Impact of High-Temperature Exposure on Metformin-Pectin Interaction-

Heat exposure is a critical consideration when assessing the compatibility of pharmaceutical formulations containing metformin and pectin. High temperatures can potentially alter the physicochemical properties of both compounds, affecting their stability and bioavailability. Studies investigating the effects of heat on metformin-pectin interaction have reported variable outcomes, with some suggesting no significant degradation or loss of efficacy, while others indicating potential alterations in drug release kinetics. Formulation strategies such as microencapsulation and controlled-release technologies may mitigate the impact of heat exposure, ensuring the stability and efficacy of metformin-pectin combinations under varying environmental conditions.

Using Metformin and Pectin for Moms-to-Be-

When moms-to-be have diabetes during pregnancy, it's tricky to manage. Metformin can help control sugar levels during pregnancy. Pectin, found in fruits and veggies, also helps control sugar after meals. Some studies show that using metformin with pectin helps control sugar levels better than just metformin alone. It might also help moms need less insulin during pregnancy.

Reaction of Metformin to High Temperatures-

Concerns regarding the stability of metformin when exposed to high temperatures have been raised, particularly in formulations such as extended-release tablets. While metformin is generally stable under normal storage conditions, heat exposure during manufacturing or storage may affect its efficacy. Studies evaluating the impact of heat on metformin, especially in combination with pectin, are necessary to ensure the safety and efficacy of this therapeutic approach.

Incorporating Anti-Diabetic Flavors with Pectin-

Pectin, a natural polysaccharide found in fruits, offers various health benefits, including its potential to modulate blood glucose levels. Incorporating anti-diabetic flavors with pectin, such as cinnamon or ginger, may enhance the palatability and therapeutic potential of formulations containing metformin and pectin. These flavorings not only contribute to taste but also possess bioactive compounds with anti-diabetic properties, synergizing with the therapeutic effects of metformin.

Clinical and Non-Clinical Evidence-

Clinical studies investigating the use of metformin with pectin in diabetes management are limited but promising. Non-clinical evidence suggests that pectin may enhance the bioavailability and efficacy of metformin by delaying its absorption and promoting its release in the gastrointestinal tract. Additionally, preclinical studies have demonstrated the potential of pectin to improve insulin sensitivity and reduce postprandial glucose levels, complementing the actions of metformin.

Potential benefits & Challenges-

The combination of Metformin & Pectin holds a novel therapeutic approach for T2DM management, offering a Mechanism of action, potential synergetic effects, and other health benefits beyond glycemic control. However, Challenges such as variability in pectin composition, dosage forms, and patient adherence need to be addressed to optimize treatment outcomes and ensure safety.

Future Directions-

Future research directions should focus on conducting well-designed clinical trials to evaluate the long-term efficacy, safety, and tolerability of Metformin and pectin combination therapy in diverse patient populations. Mechanistic studies are needed to elucidate the underlying pathways involved in their synergetic effects and

identify potential biomarkers for treatment response. Additionally, exploring novel formulations, delivery systems, and personalized approaches may enhance the therapeutic potential of this combination therapy.

Conclusion:

Using Metformin with pectin as a gummy can be a good idea. It might help control sugar levels better and make things easier during pregnancy. But we need to be careful regarding heat stability because it might change how these medicines work. Integrating anti-diabetic flavors with pectin formulations may further enhance their acceptability and efficacy. More research will help us understand better how to use metformin and pectin together safely, and the efficacy of these formulations, thereby maximizing their therapeutic potential in the management of gestational diabetes and beyond.

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Lloyd Group of Institutions

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on

nsformation Through Technology and Transdisciplinary Educatio

9th December, 2023

Certificate

o certify that Prof./Dr./Mr./Ms. Shivangi has participated and presented a **paper in** Session on the topic formulation and evaluation of Metformin vegan .....

ng **Lloyd's International Conference** on **"Transformation Through Technology and Transdisciplinary Educatio**

Organized by Lloyd Institute of Management & Technology (Pharm.), Greater Noida.

F PATRON
ohar Thairani
d Group of Institutions

CONVENOR
Prof. Vandana Aror
Chief Strategic Officer & Head
Lloyd Group of Institut

CURRICULUM VITAE

SHIVANGI

CAREER OBJECTIVE

- To secure a challenging position in regulatory affairs.
- To grow at Professional as well as Personal level.
- To use my knowledge and skills with the profit of the organization.

ACADEMIC REVIEW

COURSE	UNIVERSITY/BOARD	PASSING YEAR	PERCENTAGE
M. Pharmacy	AKTU	Pursuing	-
B. Pharmacy	BTE	2022	90.02%
D. Pharmacy	AKTU	2019	80.09%
Intermediate	CBSE	2017	76%
High school	CBSE	2015	8.4 CGPA

SKILLS

- Computer skills: MS Word, MS PowerPoint, MS Excel.
- Good communication skills
- Regulatory knowledge and Documentaion.

ACHIEVEMENTS

- Oral presentation at International Conference.
- Review Article on the Synergetic Potential of Metformin with Pectin published in IJCRT.
- Ongoing Research article for Scopus.
- License of Registered Pharmacist.

PERSONAL INFORMATION

DOB:15-02-2000

D/O: Mr. Shiv Deen Dayal Kaushik

Address: Gyan Lok Colony, Khurja, Bulandshahr Language:

Hindi, English

8279480749

shivangi15kaushik@gmail.com

I here Declare that all the information given above is true.

Shivangi

ORIGINALITY REPORT

3%	2%	0%	1%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	repository-tnmgrmu.ac.in Internet Source	<1%
2	www.intechopen.com Internet Source	<1%
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7	Niazi, . "Guidance on Formulating Compressed Solids", Handbook of Pharmaceutical Manufacturing Formulations Compressed Solid Products (Volume 1 of 6), 2004. Publication	<1%
8	perks.optum.com Internet Source	

CERTIFICATE

Certified that **Shivangi** (Enrollment no. **220227056084788**) has carried out the research work presented in this thesis entitled "**Formulation And Evaluation of Metformin Vegan Gummies For Gestational Diabetes**" for the award of **Master of Pharmacy** from Dr. APJ Abdul Kalam Technical University, Lucknow under my/our supervision. The thesis embodies the results of the original work, and studies are carried out by the student herself. The contents of the thesis do not form the basis for the award of any other degree to the candidate or anybody else from this or any other University/Institution.

Signature

Dr. Amarjeet Singh
Professor & Principal
Innovative College of Pharmacy

INNOVATIVE COLLEGE OF PHARMACY
PRINCIPAL

Signature

Mrs. Roshan Zehra
Associate Professor
Innovative College of Pharmacy

Date:

Innovative College of Pharmacy
Plot No. 5, Knowledge Park-2,
Greater Noida

(III)