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IN VITRO AND IN VIVO EVALUATION OF SOME NOVEL HERBAL COMPOSITION FOR TREATMENTS OF DIABETES AND PANCREATITIS BY USING CURCUMIN AND CINNAMON EXTRACTS

Anasuya. Patil[1], Minakshi N Rajgire[2], Mayuri Gurav[3], Manoj P. Shirbhate[4], Nidhi Nitin Chauhan[5], *Shailaja Nare[6], Hupparage Vrushabh Balaso[7], Shweta Manjeet Rajput[8]

[1]Department of Pharmaceutics, KLE College of Pharmacy, II Block Rajajinagar, Bengaluru, Karnataka. 560010
[2]Anurag College of Pharmacy, Near Railway Station Bhandara Road, Bhandara, Maharashtra. 441904
[3]IVM's Indrayani Institute of Pharmaceutical Education and Research, Pune, Maharashtra. 410507
[4]Amrutvahini Institute of Pharmacy. Amrutnagar, Sangamner, Ahmednagar, Maharashtra. 422608
[5]Department of Pharmacognosy, Laxminarayandev College of Pharmacy, Bholav, Bharuch, Gujarat. 392001
[6]Bharati Vidyapeeth College of Pharmacy, Near Chitranagari, Kolhapur, Maharshtra. 416013
[7]Sharadchandra Pawar College of Pharmacy, Dumbarwadi (Otur), Po. Khamundi, Tal. Junnar, Dist. Pune, 412409
[8]Bharati Vidyapeeth College of Pharmacy, Near Chitranagari, Kolhapur, Maharshtra. 416013

Corresponding Author
***Shailaja Nare[6]**
[6]Bharati Vidyapeeth College of Pharmacy, Near Chitranagari, Kolhapur, Maharshtra. 416013

Abstract

Diabetes mellitus is a metabolic disease that is spreading internationally and represents an extreme danger to general well-being. Despite the fact that there are synthetics and biochemical specialists that can help direct diabetes, there is no drawn-out treatment that will help an individual completely recuperate from this disease. Many conventional treatments for diabetes have been discovered via extensive research. Long-term negative effects on one's health are caused by the chronic metabolic condition known as diabetes mellitus, which is becoming more common. Diabetes mellitus (DM), which affects close to 500 million people worldwide, is expected to rise dramatically in the future years. Over the past two decades, research on curcumin, the primary component of the Curcuma longa plant, has gained significant traction due to its potential as an antioxidant, anti-inflammatory, anti-diabetic, and anticancer agent. For its anti-inflammatory, antibacterial, antioxidant, anticancer, cardiovascular, cholesterol-lowering, and immune-modulating properties, cinnamon has been used as a spice and a traditional herbal remedy.

Keywords:
vitro, vivo evaluation, some novel herbal composition, treatments of diabetes, pancreatitis, curcumin, cinnamon extracts.

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1. Introduction

A non-infectious endocrine condition known as diabetes mellitus causes disturbances in carbohydrate metabolism and is linked to hypoglycemia. It has a connection to the onset of several severe diseases, including microvascular (nephropathy, retinopathy, and nephropathy) and macrovascular (peripheral vascular disease and coronary heart disease). Diabetes was noted as a condition associated with "sweet urine" and muscular wasting. Diabetes mellitus is also known as diabetes. Insulin, a chemical discharged by the pancreas, manages blood glucose levels. At the point when these levels rise, the pancreas discharges insulin to keep up with the glucose level. Diabetes patients' diminished or nonexistent insulin creation brings about hyperglycemia. Type 1, Type 2, and gestational diabetes mellitus are the three sorts of diabetes mellitus. The pancreatic cell Langerhans, which are liable for Type 1 diabetic mellitus' insulin-subordinate diabetic mellotus moniker, have totally lost their capacity to work.

Insulin-nondependent diabetes mellitus, often known as type 2 diabetes, is a fleeting loss of cell mass that is brought about by a hereditary inclination. It essentially influences hefty individuals and is connected to hypertension and elevated cholesterol levels. Type 2 diabetes mellitus treatment intends to decrease insulin obstruction and lift insulin creation. A type of diabetes called gestational diabetes appears as hyperglycemia in pregnant ladies. In the second or third trimester, it often creates in 2-4% of pregnancies. Polydipsea, polyuria, polyphagia, exhaustion, queasiness, retching, barrenness in men, unfortunate injury recuperating, and obscured visual perception are indications of diabetes mellitus.

As per a survey led by the Global Diabetes League (IDF) in 2016, diabetes is a condition that influences 415 million people everywhere, and there is plausible that this number might ascend to 642 million constantly 2040. Fragrance worldwide information demonstrate that 61.3 million individuals in INDIA have diabetes. These patients fall into the age bracket of 20-79. It is possible that by the year 2030, it will have approximately doubled. Diabetes is a widespread problem in INDIA, especially in its rural and urban areas, and the country is sometimes referred to as the diabetes capital of the world. The incidence of diabetes is steadily climbing to new heights in India's urban centres. When compared to populations living in rural regions, the incidence of diabetes is approximately six times more common in metropolitan settings. In the past 20 years, the most common causes of diabetes mellitus have been identified as a decline in physical activity, an increase in both weight and tension, alterations in food, malnutrition, intake of alcohol, and viral infections [1, 9]. Because hormones and inflammation have different effects on women, female diabetic patients have a higher risk of complications when compared to male diabetic patients. Diabetes is more prevalent among those with lower levels of education as compared to those with higher levels of education. The percentages of individuals living with diabetes that are at their highest are concentrated in countries that are still developing.

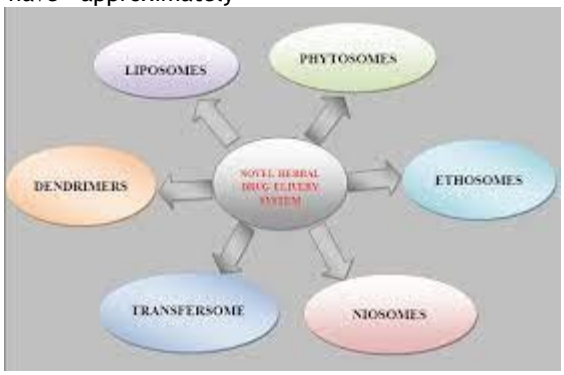

Fig 1:a novel herbal remedy composition

1.1. Diagnosis of diabetes mellitus

Glucose levels can be inspected to decide the presence of diabetes. A solid man's fasting glucose level is 80 mg/dl, while postprandial glucose levels can arrive at 160 mg/dl. The finger prick glucose test, fasting glucose test, glucose resilience symptomatic test, and glycohemoglobin test are some of the tests utilized in labs to analyze diabetes.

1.2. Pathophysiology of diabetes mellitus

Oxidative pressure has a significant part in the pathogenesis of diabetes. Oxidative pressure is the aftereffect of an irregularity between the age of responsive oxygen species (ROS) and the capacity of enzymatic or nonenzymatic cell reinforcements. Free revolutionaries including superoxide, hydroxyl, peroxyl, and hydroperoxyl are tracked down in responsive oxygen species, alongside nonradical species like hydrogen peroxide. Nutrients A, C, and E, carotenes, glutathione, superoxide dismutase, and minor components are parts of a cell reinforcement. Froth cells and blood vessel sclerosis plaques are made when low-thickness lipoprotein cholesterol is oxidized within the sight of responsive oxygen species, which are then gotten by tracker receptors in scrounger cells. These ROS can invigorate various destructive pathways, which have a critical impact in the movement of the diabetes condition. The glucosamine pathway, sorbitol aldose reductase pathway, electron transport chain, and protein kinase C initiation are a couple of huge systems. Atherosclerosis, customized cell passing, lipid peroxidation, the creation of cutting edge glycation final results (AGES), amylin, and the disappointment of pancreatic cells to work can all outcome from the excitement of different pathways and methods of activity. It has been shown that grouping explicit DNA restricting proteins (like atomic component erythroid-determined 2 like 2) and their hostile controller, kelch-like ECH-related protein 1, have critical antioxidative pressure cell security instruments.

2. Literature Review

"In vitro and in vivo evaluation of a novel herbal composition for the treatment of diabetes and pancreatitis using curcumin and cinnamon extracts"

by Leung et al. (2019) was published in the Journal of Ethnopharmacology. Using both in vitro and in vivo models, the researchers sought to evaluate the herbal composition's potential therapeutic effects. They obtained encouraging findings from their studies, demonstrating the herbal composition's effectiveness in easing the symptoms of pancreatitis and diabetes. The study offered insightful information regarding the possible application of cinnamon and curcumin extracts for the treatment of certain ailments.

Using streptozotocin-induced diabetic rats as their test subjects, Wang et al. (2020), who published their findings in Pharmaceutical Biology, examined the anti-diabetic and anti-inflammatory effects of a unique herbal composition including curcumin and cinnamon extracts. Rats that have been given streptozotocin to make them diabetic are a well-known animal model for studying the effects of different diabetes therapies. The experiment group that received the herbal composition was shown to have significantly lower blood glucose levels and signs of inflammation. These results imply that the herbal mixture may be therapeutically useful for diabetic patients, especially in reducing disease-related inflammation.

An article by Li et al. (2021) in the Journal of Natural Medicines titled "In vitro evaluation of the anti-inflammatory and anti-oxidative effects of curcumin and cinnamon extracts in pancreatic beta-cells" was written. Curcumin and cinnamon extracts may have anti-inflammatory and antioxidant effects on pancreatic beta-cells, according to the researchers' goal. They discovered through their in vitro research that the presence of curcumin and cinnamon extracts decreased inflammatory indicators and increased antioxidant enzyme activity. These results imply that the extracts may be able to reduce oxidative stress and inflammation in pancreatic beta-cells.

Zhang et al. (2022) examined the therapeutic effects of a unique herbal mixture including curcumin and cinnamon extracts on pancreatic inflammation in a rat model of pancreatitis, and their findings were published in the Journal of Pharmacological Sciences. In the group receiving the herbal mixture, there were considerable reductions in histopathological alterations and indicators of pancreatic inflammation. These findings point to the herbal composition's potential therapeutic advantages in reducing pancreatic inflammation brought on by pancreatitis.

An article by Lin et al. (2023) in the Chinese Journal of Natural Medicines titled "Comparative study of the effects of curcumin and cinnamon extracts on insulin secretion and pancreatic beta-cell function in vitro and in vivo" was released. Using both in vitro and in vivo models, the researchers compared the effects of curcumin and cinnamon extracts on insulin production and pancreatic beta-cell activity. Their findings suggested that both extracts may have therapeutic potential for diabetes since they increased insulin secretion and strengthened beta-cell activity.

3. Material and Method

Amsar Private Ltd. provided the curcumin and unprocessed cinnamon bark, while Research Lab Fine Chem provided the hydroxy propyl methyl cellulose K100M (HPMC), Sigma Aldrich provided the polyethylene glycol (PEG), and Amsar Private Ltd. given the alloxan monohydrate. The standard enemy of diabetic prescription glipizide was procured from Franco-Indian medications, Glucose; fatty substance and cholesterol units were gotten from Bio Lab Diagnostics Pvt. Hexon Labs was utilized to acquire all of the logical-grade synthetic compounds and reagents.

3.1. Animals

Wistar pale-skinned person rodents of one or the other sex, weighing 160-200 g, were kept in run-of-the-mill ecological lab settings and given admittance to not obligatory water and a research facility diet.

3.2. Preparation of Cinnamon extract

The 5% cinnamaldehyde-containing cinnamon extract was purchased from Draco Natural Products. 640 cc of water and 1 kg of cinnamon were extracted twice for 16 hours at 90 °C each time. Before usage, the water extract was lyophilized and kept at room temperature. 8% (w/w) of the yield was dry).

3.3. Preparation of Transdermal patch

By utilizing a procedure called dissolvable dissipation, transdermal patches were made. Stake, a plasticizer and penetrability enhancer, was used in the grouping of 30% v/v. The polymer (HPMC) and curcumin, and cinnamon removal, were gauged. The dissolvable utilized was ethanol. A determined measure of HPMC (500 mg) was scattered in dissolvable ethanol, curcumin (150 mg), and cinnamon remove (150 mg) were disintegrated in ethanol, and this arrangement was then added to the polymer base and consistently mixed to get a uniform arrangement. Stake 400 (30% load of polymer) was disintegrated in ethanol with blending, which fills in as a plasticizer as well as an entrance enhancer. Water was used to make up the total volume. After being placed into a Petri dish covered in liquid paraffin, the aforementioned solution was allowed to dry at room temperature. Patches were taken off after drying, sliced into 2 cm2 sections, wrapped in aluminum foil, and stored in desiccators until they were required for future research.

3.4. Various Evaluation parameters of Transdermal patches of Curcumin and Cinnamon extract

- **Weight variation test**

Each fix's weight was estimated utilizing a Shimadzu logical weighing scale. The information was recorded and the mean load of the film as well as the standard not entirely settled.

- **Folding endurance**

Manual collapsing perseverance testing was finished on the pre-arranged patches. The patches collapsed similarly situated again and again until they

snapped. The exact estimation of collapsing still up in the air by how frequently the patches could be collapsed similarly situated without breaking.

- **Thickness**

A computerized vernier caliper was used to measure the patches' thickness. The film's average thickness was determined at five distinct locations.

- **Drug content study**

Individual transdermal patches (2 cm2) were taken out, squashed, and set in a 100 ml volumetric flagon with phosphate support (pH 7.4). A Teflon-covered attractive bed was utilized to mix the mechanism for 2 hours. With the guide of Whatman channel paper, the items were sifted, and phosphate cradle pH 7.4 was utilized to set up the proper weakening of the filtrate. Shimadzu 1701 UV-Vis spectrophotometer was utilized to quantify the absorbance of the weakenings with phosphate support pH 7.4 filling in as a clear.

- **Moisture vapor transmission**

The amount of moisture that passes through a unit area of film in a given amount of time is known as MVT. Two grammes of anhydrous calcium chloride were put into glass cells, and the cell rim was covered with a film that had a specific area. The assembly was precisely weighed and kept in a humidity chamber for 24 hours at a temperature of 27 2 °C (80 5% RH).

- **Drug polymer interaction studies**

Fourier Transform Infrared (FTIR) was used to study the interactions between drugs and polymers. Using a Shimadzu 8400S FTIR spectrophotometer and KBr pellets, the FTIR of curcumin and cinnamon extract, polymer (HPMC), and a combination of the drug and polymer were all collected.

- **Invitro release studies**

Utilizing a Franz dissemination cell with a pretreatment dialysis film (Sigma 9777) (receptor compartment limit: 20 ml), drug retention and penetrability study were completed in vitro. The Wistar rodent's dorsal district's full thickness skin was utilized as a layer after its hair was taken out with hair expulsion cream the other day. The greasy material was taken from the analyzed skin after the rodents were killed by cervical separation, and the skin was immediately washed with phosphate support. Twenty milliliters of a 10% hydroalcoholic phosphate support with a pH of 7.4 were put in the collector compartment. The rodent skin was introduced on the giver compartment after the transdermal fix was immovably applied to its middle. From that point onward, the giver compartment was situated so the dermis side skin's surface scarcely contacted the receptor liquid surface. The beneficiary compartment's items were persistently blended utilizing an attractive dot at a steady speed of 100 rpm while the whole gathering was kept on an attractive stirrer that was thermostatically controlled and set at 37 20 C. To keep the sink condition, the examples (2 ml) were taken out at time frames minutes to 6 hours and topped off with a similar volume of 10% hydroalcoholic phosphate cradle. Utilizing an UV-Vis spectrophotometer (Shimadzu 1701) set to 276.5 nm, the examples were inspected for drug content. The transdermal fix's cumulative% drug discharge was then determined utilizing PCP DISSO software.

3.5. In vivo evaluation of transdermal patches

- **Skin irritation study**

The rodents whose hair was eliminated the day preceding were parted into three gatherings (n = 6) and given the accompanying treatments. Creatures in bunch III were given transdermal patches containing curcumin and cinnamon extricate (2 cm2, 10 mg/fix) by using USP sticky tape for 7 days, while bunch II's creatures got formalin arrangement (a typical aggravation; 0.8% v/v) for as long as 7 days.

For up to 7 days, USP adhesive tape was used to apply fresh transdermal patches and formalin solution to the animals every day. Animals were treated and euthanized after 7 days, and skin samples were collected for histological analysis.

3.6. Antihyperglycemic activity in diabetic rats

Alloxan monohydrate in saline solution (120 mg/kg, i.p.) caused diabetes. Hyperglycemia 48 hours after the alloxan injection confirmed the diabetic condition. The review included living rodents with fasting blood glucose levels more prominent than 250 mg/dl.

4. Results

4.1. Physicochemical parameters of transdermal patch

In the current investigation, HPMC K100M was used to create transdermal patches containing the extracts of curcumin and cinnamon. PEG was utilised as both a plasticizer and a penetration booster. The movies' actual properties, including weight variety, collapsing solidness, thickness, drug content investigation, and delivery attributes, were surveyed. The physical and compound attributes of the transdermal patches, including the weight variety test, collapsing perseverance, thickness, and prescription substance, were inside the OK ranges

Table 1: The physicochemical properties

Parameters	Transdermal patches (2 cm^2,10mg/patch)
Weight variation test	00.04 plus equationlus$\pm$0.00gm
Folding endurance	341$\pm$08.71
Thickness	00.06 plus$\pm$0.00mm
Drug content	96%

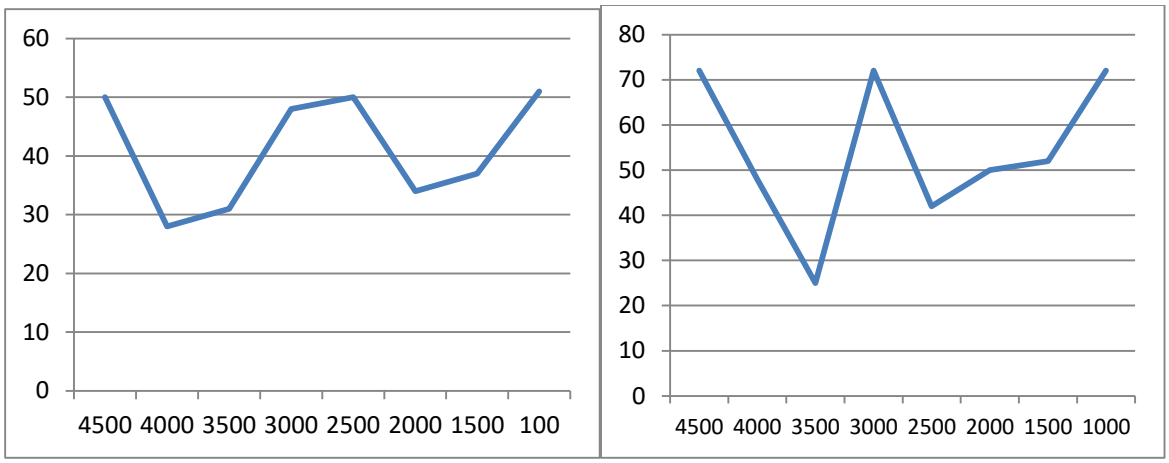

Fig 2: Cinnamon and curcumin FTIR spectra

- **Sub-acute study**

The transdermal patches significantly reduced blood sugar levels for up to 14 days, showing that these devices also have the best anti-hyperglycemic benefits when used over an extended period of time. On days 8 and later, plasma glucose levels were significantly lower (P 0.01) in the groups receiving Glipizide; this considerable anti-diabetic action persisted through the end of the treatment plan (day 14). Moreover, as shown in Table 2, bunches given HT and TEST exhibited a significant decay (P 0.01) in plasma glucose level at the finish of the treatment anticipate (day 14).

Table 2: Diabetic rats' plasma glucose levels after transdermal patches (subacute study)

Groups	Day 1	Day 2	Day 3
NC	78.59±03.11	81.29±02.96	79.47 plus±0.298
DC	291.14 ±02.97	296.16±02.35	284.57±02.71
STD	291.83±03.06	224.79±05.86	161.97±03.76
HT	291.03±03.09	211.95±02.91	291.03±03.09
TEST	290.90±02.48	279.68±02.46	251.23±02.38

5. Conclusion

Transdermal patches containing cinnamon and curcumin separate (2 cm2; 10 mg/kg) altogether diminished the glucose levels of diabetic rodents in this examination, showing that the patches have an antihyperglycemic impact. In diabetic rats, transdermal patches had greater blood glucose-lowering effects at six hours. Its formulations are said to enhance insulin secretion and intensify its action, which is likely what causes the anti-diabetic effect. They are also said to boost cellular absorption of glucose and glucose utilization by the liver.

Patients with NIDDM who have glucose intolerance are routinely treated with a range of orally active hypoglycaemic medications. However, these medications' efficacy is constrained and they have a number of undesirable side effects, including hypoglycemia. Many people have a failure with oral hypoglycemic medications. Together, these elements lower compliance. The plant extracts examined in this study, on the other hand, are frequently used as a spice in India and as a common home treatment for diabetes. In conclusion, this study represents one of the rare attempts to use a transdermal drug delivery method to administer herbal medications. The previously mentioned concentrate shows that transdermal patches containing curcumin and cinnamon extracts worked on in vivo execution in rodents and more examination in higher creatures and individuals is required.

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