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An article of transdermic medication delivery contraptions for Diabetes management

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Abstracts:
Diabetes mellitus is a chronic condition characterized by insufficient pancreatic insulin production or the body's ineffective utilization of insulin. Currently, over 415 million individuals are affected globally, with projections indicating that this number may rise to 642 million by 2040. The World Health Organization projects that diabetes will be the seventh leading cause of death by 2030. Current diabetes management strategies encompass oral hypoglycemic agents and insulin administration, both of which frequently necessitate substantial patient adherence. Transdermal systems for diabetes treatment have garnered attention in recent years as a viable alternative, offering advantages over oral medications and injections. This review presents recent advancements in transdermal research focused on enhancing diabetes management. Numerous technologies and techniques have been investigated and applied in transdermal systems for the treatment of diabetes. Research indicates that transdermal devices enhance bioavailability relative to oral delivery by circumventing first-pass hepatic metabolism and facilitating a continuous drug release pattern. Transdermal devices improve patient compliance by decreasing dose frequency and effectively regulating blood glucose levels over a prolonged duration. The transdermal system offers notable advantages compared to the oral route for the administration of antidiabetic medications and the biosensing of blood glucose levels, indicating potential improvements in clinical outcomes for diabetes management.

Keywords: Percutaneous, Diabetes. Antidiabetic, Insulin, Drug delivery system

INTRODUCTION:

Diabetes, first identified in 1500 BCE as "honey urine," has been a potentially fatal condition for almost 2000 years. Chronically elevated blood sugar is the hallmark of diabetes mellitus. Insulin dysfunction or improper release causes diabetes. [1, 2] Diabetes can be categorized based on its onset and initial manifestation upon diagnosis. T1DM patients lose insulin-producing beta cells in the islets of Langerhans, resulting in no insulin. Insulin-dependent diabetes mellitus, or Type 1A, is immune-mediated and causes beta cell death at various rates in different patient groups. Type 1B diabetes mellitus, also known as unexplained diabetes, occurs when no inflammatory mechanism destroys beta cells and there is no other recognized cause of insulin deficiency. Type 2 diabetes mellitus (T2DM), formerly non-insulin-dependent diabetes, is the most prevalent kind, affecting 90%–95% of people with diabetes. [3,4] Genes or the environment might induce insulin insufficiency and resistance in this kind of diabetes. Many individuals remain unaware that they have T2DM, a condition associated with obesity. Any glucose is too much for gestational diabetes. Regardless of its persistence, this condition first becomes apparent during pregnancy. [5]

Diabetes types and prognosis: The primary causes behind type 2 diabetes are factors such as diet and lifestyle. The proportion of type 2 diabetes is increasing in most countries, with around 374 million people at increased risk of developing type 2 diabetes. [1]

The 7th edition of the International Diabetes Federation's IDF Diabetes Atlas estimates 415 million people aged 20 to 79 have diabetes out of a worldwide population of 4.72 billion. Stated otherwise, diabetes strikes one in every eleven adults. Six forty-two million individuals with diabetes are expected to be added, or one in every 10 people out of a population of 6.16 billion by 2040. [6]

On the World Health Organization's map of regional prevalence, the 27-country Western Pacific area came forth in 2015. Of the population, diabetes affects 8.8% (7.7%-10.8%). Forecasts indicate that Southeast Asia will rank fifth in 2040, with a share of 9.0% (7.3%-11.6%).[4,7]

In 2015, diabetes claimed the lives of five million people worldwide. A typical clinical observation in diabetes is that chronic hyperglycemia greatly raises the chance of long-term malfunction or failure in many organs. The most crucially affected organs are the eyes, kidneys, heart, nerves, and blood vessels. Often connected to a higher risk of both microvascular and macrovascular problems is type 2 diabetes mellitus (T2DM). [8]

The symptoms of both types of diabetes mellitus are similar, but they differ in intensity. Type 1 diabetes mellitus has a rapid onset of symptoms, while type 2 diabetes mellitus has a more gradual development of symptoms. Hypoglycaemic drugs are used to treat type 2 diabetes, with metformin being the treatment that is suggested the most often. On the other hand, daily insulin injections often provide a continuous supply of insulin for type 1 diabetes. Some people with type 2 diabetes also use injectable insulin. [1]

Oral Hypoglycaemics drugs: In order to avoid complications, it is essential to maintain reasonable control of diabetes. The goal of diabetes management should be to improve glycaemic control beyond what is necessary to control its symptoms. Intensified therapy and maintaining near-normal blood glucose levels can significantly reduce the risk of developing retinopathy, nephropathy, and neuropathy. [5,9]
Metformin hydrochloride is an oral antidiabetic medication commonly used as the first-line treatment for type 2 diabetes. It is recommended for individuals who are overweight or obese and have normal kidney function. Unlike some other medications, Metformin does not stimulate insulin production from the pancreas. Instead, it reduces the production of glucose in the liver and improves the effectiveness of insulin in muscle and fat tissues. Metformin is primarily absorbed in the small intestine and does not bind to plasma proteins. However, its effectiveness is limited by the frequent occurrence of gastrointestinal side effects and rapid metabolism. [4,7]

Standard dosing of anti-diabetic medications has several shortcomings.
Traditional oral hypoglycemic medications present several challenges, such as a limited duration of action due to short half-lives, the need for frequent dosages, the potential for hypoglycemia, poor absorption, and elevated protein binding in certain cases. These issues lead to diminished patient adherence and decreased treatment efficacy. [2]
Over the last decade, researchers worldwide have been working on innovative and controlled delivery strategies for oral hypoglycemics to overcome the challenges associated with traditional dose forms. The main objective of these drug delivery systems is to ensure consistent distribution of the medicine in the body over a specific period. [8]

New methods of drug delivery for the sustained and regulated administration of anti-diabetic medications.
Microspheres
Microspheres or microparticles are solid spherical entities with a small size, ranging from 1 to 1000 µm. They are made up of one or more polymers in which drug particles are dispersed at either the molecular or macroscopic level. [9]
Microspheres' short retention duration at the absorption site limits their efficacy. Consequently, it would be beneficial to possess mechanisms that ensure close contact between this drug delivery system and the absorbing membrane. We can achieve this by incorporating bio adhesive properties into microspheres and forming mucoadhesive microspheres. These have a high surface-to-volume ratio, interact better with the mucus layer, and deliver drugs directly to the site where they are needed. Mucoadhesive microspheres are better at absorbing drugs and making them bioavailable. [7,9]

Nano systems
The field of nanotechnology uses materials and structures designed at the molecular scale to observe, repair, create, and regulate human biological systems at the cellular level. It pertains to the science of matter at the nanoscale scale. One aims to use the features of matter at these minuscule sizes, where it behaves differently, uncovering numerous unanticipated and intriguing applications. We refer to nanotechnology in medicine as nanomedicine. Nanotechnology is a central theme in diabetes research, with nanoparticles being particularly promising for the treatment and management of the illness. Drug delivery systems primarily use nano systems to extend or maintain drug release, enhance the bioavailability of poorly absorbable medications, improve drug stability, and provide targeted distribution to specific areas within the body. The primary oral hypoglycaemics include nanoparticles, solid lipid nanoparticles, nanostructured lipid carriers, and nanoemulsions [8-11]

Hydrogels
Hydrogels are three-dimensional polymeric networks that can absorb water and biological fluids. They are cross-linked macromolecular networks that are insoluble but capable of fast swelling in water or biological fluids. The characteristics of hydrogels are contingent upon their water content. Their physical characteristics resemble those of live tissue, mostly because of their elevated water content, pliable and elastic texture, and little interfacial tension with water or biological fluids. [12]
The ability of molecules of different sizes to penetrate (drug loading) and exit (drug release) hydrogels allows for their use as delivery systems. The primary method of drug release in hydrogel systems is diffusion due to their high permeability to water-soluble medications and proteins. We can control the release rate and mechanism from hydrogels by using parameters such as polymer composition, moisture content, crosslinking density, and crystallinity. Hydrogels can be prepared in various forms, including pH-sensitive, temperature-sensitive, and enzyme-sensitive hydrogels, among others. All stimuli-sensitive hydrogels have demonstrated effectiveness in drug delivery systems. [13]

Controlled and Sustained Administration by Oral Route

The oral route of administration is the most ancient and prevalent method of medication transport inside the body, owing to its versatility in dose forms, design, and patient adherence.The tablet form, favoured above other oral dose forms, provides unmatched convenience in administration and simplicity in industrial preparation. Nevertheless, immediate-release tablet formulations are often linked to many drawbacks, including variable plasma concentrations, adverse toxic effects, and the need for repeated dosage regimens. [17] To address these limitations, the pharmaceutical industry has achieved considerable advancements in the development of controlled and sustained release tablet formulations for several medications, instilling optimism for the future of drug delivery. The sustained release tablets decrease the frequency of dosing, improve therapeutic efficacy and avoid side effects associated with conventional tablets. Floating tablets prolong the gastric residence time of drug, thereby prolonging its duration of action and improving its bioavailability. [14-18]

Niosomes

Niosomes are vesicles made from non-ionic surfactants. They are created by combining non-ionic surfactants from the alkyl or di-alkyl poly-glycerol ether class with cholesterol, followed by hydration in an aqueous medium. Niosomes are more stable than traditional liposomal drug delivery systems because the surfactants used in their creation are more chemically stable than the phospholipids used in liposomes. [22] Phospholipids are prone to hydrolysis, which makes them less stable. Due to their non-ionic nature, niosomes have reduced toxicity and can improve the therapeutic index of medications by limiting their effects. Niosomes are very small in size, have osmotically active properties, and are stable. They can be customized in terms of composition, fluidity, and size to meet specific requirements. Niosome surfactants are biodegradable, biocompatible, and non-immunogenic. [1, 19-23]

Transdermal drug delivery systems

Researchers discovered in the late 20th century that they could use the skin, the body's largest organ that absorbs one-third of the blood, as a systemic drug route. A unique transdermal drug delivery device facilitates the delivery of medication through the skin. [24-28] This method offers several advantages over oral drug administration, such as bypassing the first-pass effect, maintaining consistent drug release, and overcoming biological barriers to absorption. Transdermal drug delivery is convenient and comfortable, requiring only weekly application. Simple dosing schedules can improve patient adherence to treatment. It is also a suitable alternative for individuals who are unable to take oral medications. Additionally, drugs that cause gastrointestinal discomfort can benefit from transdermal delivery, as it circumvents the stomach and intestines. [29] It beneficial for unconscious or nauseated patients and can also help reduce the drawbacks of oral medication delivery and first-pass metabolism. [30-34]

Transdermal Patch

A transdermal patch is a self-contained, discreet, medicated adhesive patch that offers a practical method of delivering medication for a variety of skin and body issues. The conventional method of administering drugs has several drawbacks, including the risk of toxicity, inconvenient administration, fluctuations in drug plasma levels, and lack of patient compliance. One innovative approach to achieving systemic drug absorption at a predetermined rate over an extended period is through transdermal medication delivery. The primary advantage of this medication is the reduced dose frequency, which prevents first-pass metabolism by allowing the drug to directly enter the systemic circulation. It is also suitable for elderly patients who are unable to take oral medications and can be self-administered with fewer adverse effects. Developing transdermal patches for hypoglycaemic agents could help address these issues. [23-25]

Conclusion:

Research into novel and controlled drug delivery systems has been ongoing for many years to address the limitations of conventional drug dosage forms. In conclusion, this review paper indicates that advanced drug delivery systems, including microspheres, nanoparticles, transdermal drug delivery systems, niosomes, and controlled drug delivery systems, offer significant advantages. These systems: a) decrease dosing frequency; b) enhance the bioavailability of hypoglycaemics; c) improve the physicochemical properties of drugs, such as solubility and stability; and d) mitigate side effects associated with conventional dosage forms.

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