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Formulation and evaluation of Glibenclamide transdermal gel

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ABSTRACT

The formulations were subjected to various physiochemical studies and in vitro permeation studies. The influence of β – cyclodextrin on the *in vitro* percutaneous absorption of Glibenclamide (GBM) and its combined effect with propylene glycol (PG) and oleic acid (OA) was studied using Franz-type diffusion cell using a cellophane membrane. The receiver solution was phosphate buffer (pH 7.4). The permeability study was carried out for 12 hours. To increase the aqueous solubility of GBM, it was incorporated as its inclusion complex with β – cyclodextrin. The inclusion complex was thoroughly characterized using techniques, including differential scanning calorimetry and scanning electron microscopy.

Keywords : Glibenclamide, β – cyclodextrin, propylene glycol, oleic acid,Skin permeability,Transdermal gel.

INTRODUCTION

Chemical name for glibenclamide is 5-chloro-N-[2-(4-[(cyclohexylcarbamoyl)amino] sulfonyl]phenyl]-2-methoxybenzamideGlibenclamide (INN), a second-generation sulfonylurea also known as glyburide (USAN), An antidiabetic[1] drug appears to lower blood sugar quickly by inducing the pancreas to release more insulin; however, its action depends on the pancreatic beta cells' ability to operate. islets[1]. Despite a slow drop in the insulin secretory response to the medication with chronic dosing in Type II diabetes patients, the blood glucose-lowering benefit endures. Glibenclamide and other sulfonylureas1 bind to ATP-sensitive potassium channels on the surface of pancreatic cells, decreasing potassium conductance and depolarizing the membrane. Depolarization increases intracellular calcium ion concentrations by promoting calcium ion inflow through voltage-sensitive calcium channels, which causes insulin to secrete or exocytose. HPLC estimation of glibenclamide in human serum has been documented[3]. Litrature survey describes the small-scale estimation of glibenclamide, glipizide, and metformin using ultra-rapid HPLC[2] and also describes the small-scale estimation of six anti-diabetic[4] drugs using HPLC[4]: glibenclamide, gliclazide, glipizide, pioglitazone, repaglinide, and

rosiglitazone. There are several test techniques for use in pharmacokinetic investigations to determine the presence of glibenclamide in biological samples [5, 6, 7, 8, and 9].

Uses of Glibenclamide

When diet and exercise are insufficient to control type 2 diabetes mellitus, glibenclamide is used to reduce blood sugar levels.

It helps persons with type 2 diabetes better regulate their blood sugar levels when combined with diet and exercise.

Side effects of Glibenclamide

Low blood sugar, often known as hypoglycemia Vomiting, heartburn, stomach bloating, nausea, and abdominal pain.

Transdermal gel

Both in pharmaceutical preparations and cosmetics, the usage of transdermal gels has increased[10]. In comparison to creams and ointments, transdermal administration of gels at pathological locations offers substantial advantages in a faster release of medicine straight to the site of action, independent of the drug's water solubility.According to the U.S.P., gels are a semisolid system made up of a dispersion formed of either big organic molecules or small inorganic molecules enclosed and interspersed by liquid. Large organic particles are dissolved in the continuous phase, randomly coiling in the flexible chains, while inorganic particles are not dissolved but rather scattered throughout the continuous phase in gels. A colloid that is usually 99% liquid by weight and is immobilised is called a gel. surface tension created between it and a network of fibres made up of small amounts of a gelating material[11]. Topical drug administration is a localised method of administering medication through the skin, vagina, rectal, and ocular cavities.

Advantages of transdermal gel

- They can prevent problems with gastrointestinal medicine absorption.
- They can take the place of oral medicine administration when it is not appropriate.
- In order to prevent the first pass effect.
- They have patient compliance and are non-invasive.
- They are easier to wash off the skin and are less oily.
- It's economical.
- Lower dosages when compared to oral dosing types.
- Limited side effects and a localised effect.
- Enhancing medication bioavailability and decreasing dosage frequency.
- Keeping drug delivery profiles steady.[12]

Mechanism of action

Without building up in the dermal layer, the medication first goes through the stratum corneum and then deeper layers of epidermis and dermis. Drug becomes available for systemic absorption when it enters the dermal layer through the dermal microcirculation.

Method of preparation of gel

- **Dispersion Method**

Stir the polymers in the distilled water continuously to distribute them. To create a gel, warm the colloidal viscous dispersion. Drug should be dissolved in a solvent and stirred into the gel before penetration enhancer is added. If necessary[17], add a pH adjuster to change the gel's ability to act as a buffer.

- **Cold Method**

The gelling ingredient was gradually added while being stirred throughout the entire solution. kept the temperature under 100°C. Drug was slowly and gently mixed into a solution before being added. Transfer to container right away, then let it warm to room temperature. At this point, the liquid will gel into a transparent substance.

- **Chemical Reaction**

The hydrolysis of the precursor in acidic or basic mediums and the polycondensation of the hydrolyzed products are the two key processes involved in the sol-gel technique. This results in the formation of a polymeric network where MNPs can be maintained.

- **Temperature effect**

It has been noted that if there are no changes in solubility with temperature during the sol-gel transition, gel formation should occur more quickly the higher the temperature.

- **Fusion Method**

This technique uses a variety of waxy compounds as a gellant in non-polar fluids. When waxy materials melted via fusion, drugs were added and slowly mixed until a homogenous gel formed.

Physiological evaluation

With the help of a digital pH metre, the pH of gel compositions was assessed. In 100 ml of distilled water, one gramme of gel was dissolved, then let to stand for two hours. Each formulation's pH was measured three times, with the average readings being computed.

Using a Brookfield Viscometer, the viscosity of the produced gel was measured. Using spindle number 64, the gels were revolved at a speed of 20, and the appropriate dial reading was recorded.

Drug Content

The UV spectrophotometric approach was used to assess the homogeneity of medication content across all formulations. Glibenclamide gel containing 500 mg was dissolved in 50 cc of methanol. The volumetric flask

was stored for two hours and well mixed in a shaker. The filter paper was used to filter the solution as it was being applied. At 300 nm, the drug concentration was spectrophotometrically determined using methanol as a reference.

Differential scanning calorimetry (DSC)

A baseline was obtained and used as a background for the DSC analysis. Accurately weighed samples (3–4 mg) were sealed in aluminium pans and heated at a rate of 5 °C/min. Under a nitrogen purge, the measurements were carried out at a heating range of 40–400°C. For the DSC run, a nitrogen flow rate of 20 ml/min was utilised. To confirm the formation of inclusion complex, DSC studies were carried out on GBM, CD, and GBM:CD complex samples.

In vitro permeation studies

For the in-vitro permeation research, a modified Kehshary-Chein diffusion cell was employed. As a permeability barrier, a commercially available semi permeable membrane was used in the investigation. The diffusion cell includes two compartments—donor and receptor—and a 1.76 cm2 diffusional surface area. It was made of borosilicate glass. In the donor compartment, 0.5 g of the gel was applied to the membrane surface, and 5 ml of phosphate buffer (pH 7.4) was added to the receptor.

The Analysis of permeation data

Using zero-order [13], first-order [14], and the Higuchi equation [15], the kinetics of drug release from Glibenclamide gel formulations during permeation studies in phosphate buffer pH 7.4 were calculated. The well-known exponential equation (Korsmeyer-Peppas equation), which is frequently used to describe the drug release behaviour from polymeric systems when the mechanism is unknown or when multiple types of release events are present, was also fitted to the diffusion data [16].

Scanning electron microscopy (SEM)

SEM (HITACHI S-3000N, Japan) operated at an accelerating voltage of 20 kV (filament current of 1.75 A, beam current of 30-40 mA, and probe current of 250 pA) was used to analyse the morphology of the samples. The samples were made by mounting 0.5 mg of powder onto a silicon wafer measuring 5 mm by 5 mm and attached to an aluminium stub with graphite tape. A 200 layer of a gold/palladium alloy was then sputter-coated onto the powder for 40 s while the beam current was between 38 and 42 mA.

Stability studies

The stability study entails a number of tests to guarantee the stability of a therapeutic product. The ideal gel formulation was kept in a tightly sealed stoppered glass container and kept between 5°C and 3°C and 30°C and 2°C. Data from the three-month trial on physical characteristics, content consistency, and medication permeability were collected at regular intervals**.**

CONCLUSION

Over the more conventional oral and intravenous delivery methods, the administration of medications through the skin offers a number of significant benefits. Transdermal drug delivery systems' primary goal is to deliver medications into the bloodstream through the skin at a predefined pace with little inter- and intrapatient

variability. An oral potassium channel inhibitor called glibenclamide is used to treat diabetes. Due to the first pass effect, even though it is absorbed from the gastrointestinal tract, its bioavailability is minimal. The purpose of the current study is to develop, construct, and assess a transdermal treatment system for glibenclamide that would deliver continuous glibenclamide dosing at a steady and controlled rate for a predefined amount of time. The results of the experiment indicate that Glibenclamide transdermal gel formulation can be created by employing carbopol 940 in a direct dispersion technique. The desired amount of drug flux is greatly increased by the addition of penetration enhancers. combination of ingredients The maximum penetration rates were seen with 10% oleic acid, 25% propylene glycol, and the drug's inclusion complex with beta-cyclodextrin in a 1:2 w/w ratio. Formulation F10 demonstrated a better release pattern and physiochemical properties when comparing in vitro drug release data. It was discovered that swelling controlled drug release and zero order kinetics were used to release the drugs from the formulations.

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