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REVIEW OF BILAYER TABLET CONTAINING IRBESARTAN AND METFORMIN HYDROCHLORIDE FOR DIABETIC HYPERTENSIVE PATIENTS

M. JAYAKUMAR

MASTER OF PHARMACY PALLAVAN PHARMACY COLLEGE KANCHIPURAM
261124506006

ABSTRACT:

Background:

One typical side effect of type II diabetes is hypertension. The goal of the current study was to create bilayer pills that would help those with type II diabetes who also had high blood pressure. The produced bilayer tablet contains a sustained release (SR) layer of metformin hydrochloride, an anti-diabetic medication, and an immediate-release layer of irbesartan, an anti-hypertensive medication. These bilayer pills were designed to combine two different monotherapies into a single combination therapy in order to improve patient compliance.

Methodology:

For a twelve-hour drug release, a variety of polymer ratios, such as HPMC K100M, EC, Eudragit, and Guar gum, were used. Spherical agglomeration was used to create an irbesartan immediate-release layer. The produced bilayer tablets' stability, release kinetics, solubility profiles, physical characteristics, and drug content were evaluated.

Keywords: Bilayer tablets, Diabetes, Hypertension, Sustained release, Immediate release

INTRODUCTION:

The significant prevalence of hypertension and its association with an increased risk of cardiovascular disease make it a major global health concern. (1,2) Significantly, the notable declines in the death rates from heart disease and stroke in developed nations can be attributed to advancements in the detection and treatment of hypertension. However, in recent years, high blood pressure control rates have decreased in several of these nations. (3.4) ACE inhibitors, calcium antagonists, angiotensin-II antagonists, β-blockers, diuretics, and α-adrenergic blockers are the main pharmacological types used to lower blood pressure. (5.6)
High blood pressure is a prevalent issue among adults and the elderly in both industrialized and developing nations. Numerous pharmacological classes are available to treat this illness and prevent its consequences, which are more common in individuals with metabolic syndrome and/or Type 2 diabetes in addition to the previously stated patients.

Higher patient complications and improved therapeutic management are made possible by the medication's efficient, long-term use in controlled drug delivery systems, which also have a very low risk of toxicity. Among the many characteristics that make a medication delivery system effective, bi-layer tablets mark a new era in the development of controlled release formulations. Seven (7)

ORAL DRUG DELIVERY SYSTEM:

The oral route has long been the preferred method of medication delivery since it provides a useful method for effectively achieving both systemic and local effects. It is still the suggested method of administration that is considered when developing new medication formulations and candidates. The oral route is popular due to patient acceptance, convenience of administration, accurate dosage, cost-effective production methods, and a longer product shelf life overall. Devices for fast release medication delivery allow for rapid drug absorption. Traditional oral drug administration techniques offer relatively little control over the medication's distribution.

IRBESARTAN:

Angiotensin II receptor antagonists are primarily used to treat high blood pressure. It primarily inhibits angiotensin II receptor type 1 and is a nonpeptide tetrazole derivative that is taken orally. C25H28N6O is the chemical formula, and its molecular weight is 428.53 g/mol.

Many conditions, including hypertension, heart failure, myocardial infarction, and diabetic nephropathy, have been treated with angiotensin II receptor type 1 antagonists.

A higher frequency of stroke and coronary heart disease is also linked to hypertension, which is a risk factor for cardiovascular disease in and of itself. Blood pressure regulation is mostly dependent on the renin-angiotensin-aldosterone system (RAAS). When blood pressure, salt levels, or renal blood flow decline, the kidney releases the proteinase enzyme renin.

With its unique pharmacological properties and good antihypertensive performance, irbesartan is a medication belonging to the angiotensin-receptor blocker class. Its effectiveness has been further assessed in patients with metabolically complicated hypertension. The authors of this study will examine its efficacy in preventing or postponing organ damage in hypertensive patients, paying particular attention to the financial effects of using irbesartan to treat hypertension in light of the availability of antihypertensive medications.

METFORMIN HYDROCHLORIDE:

One of the most commonly given medications in the world for a number of purposes is metformin. While metformin offers several significant benefits, such as ease of administration and storage, it also has a high rate of gastrointestinal adverse effects. Since there isn't enough systematic data to support head-to-head comparisons of various metformin formulations, slower-release forms of the medication may be less likely to cause side effects while still being effective.

Metformin works by reducing intestinal glucose absorption, hepatic glucose synthesis, and insulin sensitivity.
The main reason metformin is administered is as an oral glucose-lowering medication for type 2 diabetic mellitus (T2DM). The long-term effects of diabetes can be reduced by using metformin to treat hyperglycemia (8).

Other reasons for which metformin is prescribed include obesity [11], gestational diabetes [10], and polycystic ovarian syndrome (PCOS) [9], albeit these uses are not authorized in the United Kingdom or the United States. A growing amount of data also points to the potential benefits of metformin for a variety of ailments, including preeclampsia [14], dermatological disorders [13], and cancer treatment [12].

Mechanism of Action:
The angiotensin-converting enzyme (ACE, kinase II) catalyzes the reaction that converts angiotensin I into angiotensin II, a powerful vasoconstrictor. The main pressor of the renin-angiotensin system (RAS), angiotensin II also promotes the proliferation of smooth muscle cells, heart contraction, renal reabsorption of sodium, sympathetic nervous system activity, and the synthesis and secretion of aldosterone by the adrenal cortex. Irbesartan selectively binds to the AT1 angiotensin II receptor, blocking the vasoconstrictor and aldosterone-secreting actions of angiotensin II. Although the AT2 receptor is present in numerous organs, cardiovascular homeostasis is not impacted by it.

Bilayer tablets:
The goal of pharmaceutical tablet producers has long been to identify and improve the method used to create double-layer tables. There are always special considerations to be made when creating a standard procedure for a repeatable manufacturing process, regardless of whether it is motivated by capacity requirements, marketing-based concepts, or basic physics.

In particular, the development of a single solid dosage form has long been considered a process that is better characterized as an art form. Bi-layer or double-layer tablets have been in use recently. This dosage form's first applications were presumably motivated by marketing considerations, with a focus on the consumer's perception of the product.

Potential Reason for Considering the Double-layer Dosage Form:

- One of the more popular justifications for wanting to produce double-layer products is the difference between sustained and quick release active ingredients, as well as the corresponding bioavailability of each in the human body.
  The In certain situations, the manufacturer intends to create products that contain two distinct active ingredients: one with an immediate release pharmacological effect that the body can start using right away, and another with a sustained release pharmacological effect that takes place over a longer period of time.
- These two functions can be neatly delivered in the same tablet by separating the actives into two distinct layers.

Bilayer problems:

- Layer-separation.
- Insufficient hardness.
- Inaccurate individual layer weight control.
- Cross contamination between the layers.

- Reduced yield.

Bi-Layer tablets: Quality and GMP-requirement:

To produce a quality bi-layer tablet, in a validated and GMP-way, it is important that the selected press is capable of-

- Preventing capping and separation of the two individual layers that constitute the bi-layer tablet.
- Providing sufficient tablet hardness.
- Preventing cross-contamination between the two layers.
- Producing a clear visual separation between the two layers.
- High yield
- Accurate and individual weight control of the two layers.

Conclusion:

The combination of Irbesartan and Metformin in bilayer tablets demonstrated stability, regulated drug release, and the desirable physical attributes. Patients with diabetes and hypertension may benefit from this formulation, which offers reliable and efficient treatment of both conditions while enhancing patient adherence. For people with type 2 diabetes, metformin offers several advantages. It has a beneficial impact on lipid profiles, improves vascular and hemodynamic indicators, and successfully lowers HbA1c levels. The majority of adverse effects are manageable and self-limiting. Products that combine metformin with rosiglitazone or a sulfonylurea have been available, broadening the range of treatments available for type 2 diabetes. In order to manage hypertension in people with type II diabetes, the study developed bilayer tablets with irbesartan (IR layer) and metformin hydrochloride (SR layer) to increase patient compliance.

. Wet granulation techniques resulted in high precompression flowability because to the granules' weak flow characteristics. The tablets met all of the specifications for friability, thickness, diameter, hardness, and weight consistency.

RESULTS AND DISUCSSION：

With bulk and tapped densities ranging from 0.39-0.46 g/cm³ and 0.42-0.55 g/cm³, respectively, the analysis of SR granules and bilayer tablets produced exceptional packing qualities and excellent flow properties. According to in vitro dissolution testing, irbesartan was initially released from the immediate-release layer. At higher polymer concentrations, the metformin sustained-release layer nevertheless demonstrated regulated drug release over a 12-hour period. Stability testing revealed that the bilayer tablets' dissolving profiles, medication content, and physical characteristics remained mostly unchanged.

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