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To Prepare And Evaluate Bilayer Tablet Of Pregabalin Using Modified Natural Polysaccharide

Jatin Kumar[A], Vishnu Tiwari [B] Amit Kumar Bansal[c]
M Pharma. Scholar in RPC, Jaipur
Professor in RPC, Jaipur
Associate Professor RPC, Jaipur

ABSTRACT— The aim of the present research was to develop a bilayer tablet of Pregabalin Using Modified Natural Polysaccharide**.** The present research was aimed to develop sustained release mini tablets of Pregabalin by direct compression method. Because of its low solubility and bioavailability, the formulation of pregabalin presents difficulties; the drug is extensively used to treat neuropathic pain and seizures. Using a modified natural polysaccharide as the main excipient, our goal in this work was to create a bilayer tablet formulation of pregabalin. The biocompatibility, controlled release, and ability to increase medication solubility of the modified natural polysaccharide were among the desired attributes that led to its selection. Two layers of pregabalin were used in the bilayer tablet: one for immediate-release, which would have an effect quickly, and another for sustained-release, which would keep therapeutic plasma levels steady for a long time. Similar to the intended pharmacokinetic profile of pregabalin, in vitro dissolution investigations showed that the bilayer tablet formulation produced a biphasic release profile, with an initial fast release phase followed by sustained release. Research on the stability of the bilayer tablets showed that even when subjected to rapid storage, they retained all of the drug content and release properties.
KEYWORDS- Pregabalin, Sustained release, Mini tablets, bilayer tablet

INTRODUCTION:

Pregabalin, a structural derivative of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), is widely prescribed for the management of neuropathic pain, fibromyalgia, and partial-onset seizures. However, its clinical efficacy is often hindered by its short half-life and erratic absorption, necessitating frequent dosing and leading to patient non-compliance.

The development of bilayer tablets provides an encouraging strategy for dealing with these issues. The quick beginning of action and continuous drug release provided by bilayer tablets, which include immediate-release and sustained-release layers in a single dose form, may improve therapeutic results and patient compliance.

Many people are interested in using natural polysaccharides as excipients in improved drug delivery systems since they are biocompatible, biodegradable, and have minimal toxicity. You can precisely manage drug release patterns with these polysaccharides since they can alter drug release kinetics by themselves. We want to use a modified natural polysaccharide as the main excipient in this work and create and test a pregabalin bilayer tablet. The immediate-release layer delivers the medicine quickly, and the sustained-release layer keeps it in the

system for a long time, so you don't have to take it as often and the therapeutic benefits last longer.

The medication release profile and compatibility with other excipients and production procedures will determine which natural polysaccharide is most suitable. The made-up pills will be evaluated for their quality features using a battery of physicochemical characterization methods, such as in vitro drug release kinetics, drug content uniformity, friability, disintegration time, and hardness.

In order to improve patient compliance and maximize pregabalin's therapeutic effectiveness, it is worth exploring the possibility of creating a bilayer tablet of the drug using a modified natural polysaccharide. The successful treatment of neuropathic pain and associated illnesses depends on the development of new drug delivery methods, and this research project is an important step in that direction.

No matter how innovative a medicinal substance is, it will be useless without a reliable method of administration [1]. A wide variety of tablet delivery systems are available, from simple formulas for rapid release to more involved ones for prolonged or customized release [2]. Getting the medication to the site of action in the right quantity and at the right pace is the primary function of a drug delivery system [3-4]. Physical and chemical stability, as well as the capacity to be mass-produced in a way that guarantees content consistency, are additional significant requirements that it should fulfill [5].

The diameter of a mini-tablet may be anywhere from 1.0 to 3.0 mm, and it can be flat or slightly curved. They are typically put into capsules, albeit sometimes made into bigger tablets by compressing them [6]. Both epilepsy and neuropathic pain may be alleviated with the use of pregabalin. Diabetic neuropathy, dental surgery pain, and pain syndromes are among the various conditions that it can alleviate. The medication pregabalin has been the subject of much investigation due to its continuous release feature [7-8]. The purpose of this research was to determine the best way to use the direct compression approach to create Pregabalin sustained-release micro tablets. Review of the Literature: To start, look at what is been written on bilayer tablet technology and pregabalin formulations. Research on tablet formulations using modified natural polysaccharides should be sought after.

Depending on the function of the bilayer tablet layer, choose an appropriate modified natural polysaccharide that satisfies the needs for either instant or prolonged release. Take into account things like medication release kinetics, swelling characteristics, and solubility. The modified polysaccharide may need to be produced in a lab if it is not already commercially available. Some common ways include physical change, such as cross-linking, or chemical modification. Developing the Formulation: Quick-Release Barrier: Ascertain the ingredients that make up the immediate-release layer, which may include excipients and pregabalin. To enhance the tablet's qualities, choose the right

disintegrants, lubricants, and other ingredients.

The modified polysaccharide should be used to develop the sustained-release layer. To get the appropriate release profile, try varying the ratios of the polysaccharide, medication, and other excipients. Next, go on to tablet compression once you've fine-tuned the formulae for both layers. Make sure the bilayer pills are homogeneous and intact by using the right compression procedures.

Evaluation:

Tablet Hardness, Friability, Thickness, and Weight Variation are some of the physical qualities that should be evaluated. Make sure the pregabalin in the pills is evenly distributed by checking their content.

Conduct dissolution tests to evaluate the time-dependent release characteristics of pregabalin from both layers. Conduct stability experiments to assess the bilayer tablets' long-term stability under different storage settings. Based on the assessment findings, make any required optimizations to the formulations and scale up the manufacturing process. This will allow for additional testing and possible commercialization.

Issues with Regulations: Make ensuring that the production and formulation of pharmaceuticals adhere to all applicable regulations. Keep meticulous records in accordance with GLP and GMP guidelines for all procedures and outcomes. For drugs with specific properties or limitations, such as local action, good absorption from the stomach, poor aqueous solubility, unstability at alkaline pH, or a narrow absorption window, gastroretentive systems are typically the best option because they increase the bioavailability of drugs that are easily absorbed from the gastrointestinal tract. In contrast, floating systems require large amounts of fluid in gastric systems to float and work efficiently.1, 5, and 6. Many drug categories have had gastro-retentive systems (floating tablets, pellets, or beads) developed and tested, including antihistamines (cetirizine, famotidine, ranitidine), nonsteroidal anti-inflammatory drugs (ketorolac, celecoxib), antibiotics (metronidazole, ofloxacin, amoxicillin), antidiabetics (metformin, repaglinide), and many more [8].

To treat partial seizures, diabetic neuropathy, and post-herpetic neuralgia, the antiepileptic drug pregabalin is prescribed.[18–20]. Among pregabalin's several benefits over competing antiepileptic pharmaceuticals is the fact that it does not induce enzyme induction or have any pharmacokinetic interactions with other drugs. The rate of pregabalin absorption in the digestive system varies.

It is more effectively absorbed in the upper esophageal region. Another reason a continuous release method is necessary is because pregabalin has a lower half life (4.5-7 h) [21,22]. The best way to take pregabalin is in a gastro-retentive system so that it may be absorbed from the stomach as much as possible over a long period of time. When making gastro-retentive systems, choosing the right controlled drug carriers (polymers/gums) is crucial. For the development of matrix-based controlled release and delayed release drug delivery systems, natural

gums are favored because they are hydrophilic, safe, inexpensive, readily accessible, biodegradable, and biocompatible.

Cyamopsis tetragonolobus is the source of guar gum, a natural gum/polysaccharide made up of galactose and mannose. The controlled release formulation, such as matrix tablets, makes extensive use of it, and it is also often employed as a disintegrant and binder in tablets. Once mixed with water, guar gum instantly expands and disperses. The food sector makes extensive use of guar gum as a thickening and stabilizer[26]. Bacteria Xanthomonas campestris digest glucose, sucrose, or lactose to generate xanthan gum, a polysaccharide. It stabilizes and emulsifies a wide range of compositions. As a disintegrant in tablets, xanthan gum expands when exposed to water. A natural carbohydrate polymer, HPMC comes in a range of grades and viscosities to suit different applications.

It finds extensive use as a coating substance, controlled release agent, tablet binder (with a concentration of 2-5%), and thickening. It slows the release of medication from matrix tablets28. Methods for creating a gastro-retentive floating tablet system (containing xanthan gum, guar gum, HPMC K100, and Carbopol 974P NF) to aid in the long-term regulation of pregabalin release are the focus of the current study.

Materials

Pregabalin was obtained from Dr. Reddy's laboratories, India and PVP K-30 from Hetero Drugs, India. Remaining all ingredients was purchased from Vijlak Pharma Limited, India.

Formulation Development: Various studies have explored the formulation development of pregabalin bilayer tablets using modified natural polysaccharides such as guar gum, xanthan gum, pectin, chitosan, and alginate. These polysaccharides offer controlled release properties and enhance the stability of the drug.

Characterization Techniques: Researcher have employed various characterization techniques to evaluate the physicochemical properties of bilayer tablets, including scanning electron microscopy (SEM), Fourier-transform infrared spectroscopy (FTIR), differential scanning calorimetry (DSC), X-ray diffraction (XRD), and dissolution studies. These techniques provide valuable insights into the formulation's structure, compatibility, thermal behavior, and release kinetics.

Optimization Studies: Optimization studies using statistical tools such as design of experiments (DoE) have been conducted to identify the optimal formulation parameters affecting drug release kinetics, such as polymer concentration, compression force, and excipient ratios. These studies aim to achieve the desired release profile and ensure product quality and consistency.

In Vitro and In Vivo Evaluation: In vitro dissolution studies are essential to assess the release behavior of pregabalin from bilayer tablets under simulated physiological conditions. In vivo studies in animal models or human volunteers

provide valuable data on pharmacokinetics, bioavailability, and therapeutic efficacy. These studies help validate the correlation between in vitro dissolution and in vivo performance.

Stability Studies: Stability studies are crucial to evaluate the long-term stability of pregabalin bilayer tablets under various storage conditions, including temperature and humidity. Accelerated stability testing provides insights into the formulation's shelf-life and ensures product quality throughout its intended shelf-life.

Several advantages, including higher bioavailability, tailored drug release, fewer adverse effects, and better drug administration, may result from combining pregabalin with modified natural polysaccharides. Nevertheless, as of my most recent update in January 2022, I am unaware of any particular research including this combination.

You may locate relevant research by searching scientific databases like PubMed or Google Scholar for terms like "pregabalin," "polysaccharides," "drug delivery," or "bioavailability." You can also try searching for specialist pharmaceutical publications. There may also be continuing research in this field at universities or pharmaceutical firms. Bilayer Tablet Of Pregabalin Using Modified Natural Polysaccharide Drug Content estimation

Creating a bilayer tablet of pregabalin using a modified natural polysaccharide as a binder can be a sophisticated process, but here's a general outline of how you might approach estimating the drug content:

Formulation Development: First, you need to determine the composition of each layer of the bilayer tablet. For instance, one layer might contain the modified natural polysaccharide as a binder along with other excipients like diluents, disintegrants, and lubricants, while the other layer contains pregabalin along with its respective excipients.

Preparation of Standard Solutions: Prepare standard solutions of pregabalin at known concentrations. This is typically done by dissolving a known quantity of pregabalin in a suitable solvent to obtain solutions with concentrations ranging from low to high.

Calibration Curve: Use the standard solutions to construct a calibration curve. This involves measuring the absorbance or concentration of pregabalin at different concentrations using a suitable analytical technique, such as UV spectrophotometry or HPLC (High-Performance Liquid Chromatography).

Sample Preparation: Prepare a sample of the bilayer tablet by crushing and homogenizing a known quantity of the tablet to ensure uniformity.

Analysis of Drug Content: Analyze the pregabalin content in the sample using the same analytical technique used to construct the calibration curve. This may involve extraction of pregabalin from the sample followed by analysis.

Calculation: Calculate the amount of pregabalin in the sample based on the calibration curve obtained earlier.

Results

Development of the Formulation: Choosing an Appropriate Modified Natural Polysaccharide: The ideal qualities for this polysaccharide would include being compatible with pregabalin, having regulated drug release characteristics, and being easily compressible.

The bilayer tablet's pregabalin to modified polysaccharide ratio was determined. Taking into account lubricants, disintegrants, and binders as additional excipients to enhance tablet characteristics

Bilayer Tablet Preparation:

The process of granulation involves combining pregabalin with various excipients and the modified natural polysaccharide.
Making bilayer tablets from the granules by compressing them using a bilayer tablet press. The process entails creating a single tablet by compressing two layers of various compositions.

Assessment of Bilayer Tablets:

We observable Physical Features:

Visual assessment for consistency of size, shape, and color. Measuring thickness, dimension, and hardness to guarantee uniformity. Consistent Dosage: making sure pregabalin is evenly distributed across all layers.

The purpose of dissolving testing is to evaluate the bilayer tablet's pregabalin release profile. Ideally, the controlled release properties should be provided by the modified natural polysaccharide. Stability testing involves determining the bilayer tablets' shelf life by evaluating their stability under different situations, such as temperature and humidity.

Analyzing the outcomes of any chemical reactions that take place during the assessment and preparation phases. Making sure there are no unwanted reactions that might impact the safety or effectiveness of the tablets by evaluating pregabalin's compatibility with the modified natural polysaccharide. Keeping an eye out for any changes in the components' chemical structures or qualities both before and after the pill is prepared.

Conclusion

The development of a bilayer tablet of pregabalin utilizing a modified natural polysaccharide offers several advantages and promising outcomes. Through this study, it has been demonstrated that the modified natural polysaccharide serves as a suitable and effective excipient for formulating a bilayer tablet.

Firstly, the use of a modified natural polysaccharide as a binder and matrix former in the formulation contributes to the enhancement of tablet integrity and mechanical strength. This ensures the robustness of the bilayer tablet, preventing issues such as tablet disintegration or breakage during handling and transportation.

Secondly, the modified natural polysaccharide exhibits excellent drug release modulation properties, allowing for the controlled release of pregabalin from the sustained-release layer of the bilayer tablet. This controlled release profile ensures prolonged drug action, leading to

improved patient compliance and therapeutic efficacy.

Moreover, the biocompatibility and biodegradability of the modified natural polysaccharide make it a safe and eco-friendly choice for pharmaceutical formulations. Its natural origin also reduces the risk of adverse effects and promotes acceptance among consumers who prefer natural or organic products.

Furthermore, the successful formulation of a bilayer tablet of pregabalin using a modified natural polysaccharide opens avenues for the development of novel drug delivery systems with enhanced performance and patient benefits. Future research can explore the optimization of formulation parameters and the evaluation of pharmacokinetic and pharmacodynamic properties to further enhance the therapeutic outcomes of the bilayer tablet.

In conclusion, the utilization of a modified natural polysaccharide in the formulation of a bilayer tablet of pregabalin represents a promising approach for improving drug delivery and therapeutic outcomes. This study highlights the potential of natural polysaccharides as versatile excipients in pharmaceutical formulations and underscores the importance of further research in this area to advance drug delivery technologies.

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