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ABSTRACT

Rifaximin, a derivative of rifamycin, has emerged as a promising therapeutic tool in gastroenterology. This review explores rifaximin's intricate molecular structure and pharmacokinetic properties, highlighting its minimal systemic absorption and targeted action within the gut. The multifaceted mechanisms of action, including direct antibacterial effects and modulation of gut microbiota, are discussed. The review then examines the efficacy of rifaximin in treating various gastrointestinal disorders like traveler's diarrhea, Irritable Bowel Syndrome with Diarrhea (IBS-D), and Small Intestinal Bacterial Overgrowth (SIBO). Dosage recommendations and the well-tolerated safety profile of rifaximin are presented. Finally, the importance of quality control measures using techniques like HPLC and spectroscopy is emphasized to ensure the drug's effectiveness and safety.

Keywords: Rifaximin, pharmacokinetics, antibiotic, analysis, traveler's diarrhoea.

I. INTRODUCTION

Semi-synthetic rifamycin derivative rifaximin has become a novel medicinal drug with an expanding array of uses in gastrointestinal illnesses. This review explores the complex properties of rifaximin by examining its composition, known applications, putative modes of action, and existing test techniques. We start by examining the molecular structure of rifaximin, emphasising the essential components that give rise to its distinct characteristics. Next, we go over rifaximin's recognised uses, emphasising how it can be used to treat illnesses like hepatic encephalopathy, traveler's diarrhoea, and irritable bowel syndrome with diarrhoea (IBS-D). This review's primary focus is on rifaximin's mode of action. We will examine the suggested processes, such as the possible modification of gut microbiota and the suppression of bacterial RNA synthesis. We'll assess the data for these mechanisms rigorously and talk about any current studies looking into other paths. Lastly, we shall discuss the rifaximin assaying procedures used at the moment. In order to assess pharmacokinetics and treatment efficacy, methods for measuring drug concentration in biological samples will be covered in this section.

In order to provide a fuller understanding of this versatile therapeutic drug and its potential to improve gut health, this review paper thoroughly examines the structure, applications, mechanism of action, and test methods of rifaximin.

II. STRUCTURE

The chemical molecule rifaximin has a complex and massive molecular structure. Rifaximin belongs to the class of rifamycin antibiotics and shares a core structure with rifampin. Its chemical formula is \( \text{C}_{43}\text{H}_{51}\text{N}_{3}\text{O}_{11} \) and its molecular weight is 785.891 g/mol. The benzopyranochromene structure makes up this nucleus [1]. Rifaximin is a crystalline powder with a cream colour and a bitter taste. The molecular weight is comparatively high at about 786 grammes per mole. Its solubility in organic solvents like methanol and ethanol is higher than its solubility in water. Rifaximin has an extremely high
Rifaximin, used for traveler's diarrhea, appears as a treatment for intestinal problems because of its low absorption into the bloodstream and strong antibacterial activity in the intestines. Studies have shown it to be effective in a variety of situations. For irritable bowel syndrome and diarrhea (IBS-D), studies such as a 2014 study in Nature Reviews Gastroenterology and Hepatology have shown that they reduce bloating and symptoms by balancing gut bacteria [3&4]. In patients with cirrhosis, a 2023 Cochrane review found that rifaximin is effective in preventing the recurrence of hepatic encephalopathy by reducing ammoniaproducing gut bacteria [5]. Similarly, a 2017 metaanalysis in the European Journal of Gastroenterology and Hepatology showed that rifaximin was successful in treating small intestinal bacterial overgrowth (SIBO) by eliminating the predominant bacteria that cause symptoms [6]. Overall, rifaximin has the potential to change the treatment of several gastrointestinal diseases due to its action focused on the intestinal tract.

MECHANISM OF ACTION

1. Coordinate Antibacterial Impact:
   Rifaximin functions as an antimicrobial agent belonging to the rifamycin family. It binds to the beta subunit of bacterial DNA-dependent RNA polymerase, a crucial molecule for RNA synthesis [7]. This individual disrupts the process of RNA translation, which hinders the growth and spread of bacteria [8]. Ask about rifaximin's properties that combat a broad spectrum of gram-positive and gram-negative bacteria, particularly those typically present in the gut.

2. Balance of Intestine Microbiota:
   In addition to directly killing bacteria, rifaximin may also affect the microbiota in the large intestine. Although the specific elements are still being investigated, several theories include:
   Specific Focusing on:
   Rifaximin primarily affects bacteria in the intestinal lumen, or the centre of the digestive tract, and has less of an impact on beneficial microorganisms that live in the intestine divider because of its poor systemic absorption [10]. This might have an impact on maintaining a healthy intestinal greenery balance.
   Anti-inflammatory Impacts:
   According to considerations, rifaximin may activate the cellular pathway involved in directing aggravation, the pregnane X receptor (PXR) [11]. This activation may trigger an explosive response in diseases such as irritable bowel syndrome (IBS-D).

DOSE

The amount of rifaximin needed differs based on the specific condition it's treating. Here are a few examples: Treating traveler's diarrhea: A study that randomly assigned participants to receive either rifaximin in doses of 600 mg or 1200 mg daily, or a placebo, found that both higher doses were more effective than the placebo in reducing the length of time someone had diarrhea while traveling [12]. Another study showed that taking rifaximin in doses of 400 mg twice daily was equally as good at relieving symptoms as another antibiotic, ciprofloxacin [13]. The typical course of treatment for Irritable Bowel Syndrome with Diarrhea (IBS-D) is taking 400 mg three times daily for a period of two weeks, as per studies. Treating Small Intestinal Bacterial Overgrowth (SIBO): A study looking into the best dose for treating SIBO found that taking higher doses (600 and 800 mg) was less effective than taking 1200 mg daily for 10 days, which led to a higher rate of normalization [15].

PHARMACOKINETICS

Derived from rifamycin, rifaximin is a non-systemic antibiotic with special pharmacokinetics that make it useful for treating gastrointestinal disorders. It acts locally in the gut after oral administration since it is only slightly absorbed from the gastrointestinal tract and has a systemic bioavailability of less than 0.4%. Food consumption has no discernible impact on its absorption [16]. About 67.5% of rifaximin binds to plasma proteins whereas it is concentrated in the gastrointestinal system with low plasma concentrations. The CYP3A4 enzyme is the main mechanism by which the small amount that is absorbed is metabolised in the liver [17]. The drug's localised effect in the gut is highlighted by the fact that most excretion happens through the faeces, where 97% of the drug is eliminated undisturbed, and less than 0.01% is eliminated in the urine [18&19]. Rifaximin is useful in the treatment of hepatic encephalopathy, IBS-D, and traveler’s diarrhoea because of its pharmacokinetic qualities.

SIDE EFFECTS

Rifaximin is typically well tolerated due to its low systemic absorption. However, a few unfavourable results of clinical research have been reported. According to a study by Pimentel et al. (2006) [20], headache (8.3%), nausea (9.8%), and abdominal discomfort (10.3%) were the most frequent side effects of rifaximin for IBS-D.
Most of these effects were mild and transient, and adverse events accounted for the majority of the study's placebo-like dropout rates.

VIII. QUALITY ANALYSIS

The effectiveness, safety, and purity of rifaximin are evaluated using a variety of analytical methods to make sure the medication satisfies requirements. By identifying contaminants and degradation products, HPLC is widely used for purity assessment and quantification. Accuracy, precision, specificity, and robustness are among the factors that are included in the HPLC method validation [16]. By comparing absorption spectra with reference standards, rifaximin's identity is confirmed using UV-visible and infrared spectroscopy. The chirality and purity of the substance are verified by measurements of optical rotation, preserving its stereochemical characteristics [17].

Additionally, a variety of matrices can benefit from the sensitive detection and quantification capabilities of fluorescence spectroscopy [16]. When combined, these analytical methods ensure that rifaximin satisfies the stringent quality control requirements required for its intended medical use.

IX. SPECTROMETRIC ANALYSIS OF RIFAXIMIN

Spectrometric examination of rifaximin uses many techniques, including UV-visible, infrared (IR), and fluorescence spectroscopy, to provide unique information on the chemical composition, purity, and concentration of the drug. The π-π* transitions in the conjugated aromatic system of the molecule are represented by the absorption peaks of rifaximin, which are located between 334 and 443 nm in UV-visible spectroscopy [21].

This technique is essential for evaluating rifaximin in pharmaceutical products because it provides a simple and reliable way to measure concentration and guarantee quality control. IR spectroscopy is used to identify particular functional groups in rifaximin; strong absorption bands are seen at about 3500 cm⁻¹ for O-H stretching, 1650 cm⁻¹ for C=O stretching, and 1600–1500 cm⁻¹ for aromatic C=C stretching [17].

These bands confirm the essential structural characteristics of rifaximin and can be used to detect deviations from the conventional formulation. Fluorescence spectroscopy is an effective tool for studying rifaximin; it provides high sensitivity for detecting and quantifying rifaximin in complex samples, with excitation at 334 nm resulting in emission peaks at about 450 nm [16].

Together, these spectrometry techniques are essential for ensuring the safety and efficacy of rifaximin when used for medicinal reasons since they facilitate analytical characterisation and quality control.

REFERENCES


X. CONCLUSION

Rifaximin has established itself as a valuable tool in the gastroenterologist's arsenal. Its unique structure minimizes systemic absorption while effectively targeting gut bacteria. Clinical applications extend beyond traveler's diarrhea, demonstrating efficacy in hepatic encephalopathy, IBS-D, and potentially SIBO. The proposed mechanisms of action, including inhibition of bacterial RNA synthesis and modulation of gut microbiota, provide a framework for understanding its therapeutic effects. However, further research is needed to fully elucidate these mechanisms and explore the drug's potential in other gut-related disorders. Continued development of sensitive assay methods will be crucial for optimizing treatment regimens and monitoring therapeutic efficacy. As our understanding of the gut microbiome and its role in health and disease continues to evolve, rifaximin's targeted approach holds promise for personalized medicine strategies aimed at restoring gut health.

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