

REGULAR ARTICLE

Study on Prescription Technology of Sofosbuvir/ledipasvir Tablet

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Abstract: Clone the Harvoni™(Sofosbuvir/Ledipasvir) tablet manufactured by Gilead Sciences, Inc. and screen out the best formula of prescription, to make the pesticide effect of prepared tablet was equal to the original tablet. Methods: Based on the prescription of Harvoni™ manufactured by Gilead Sciences, Inc., the compatibility test of the excipient with the active ingredient was carried out. The stability of self-made samples and reference preparations were investigated, which includes high temperature, high humidity and light conditions. According to the above test, the most reasonable prescription process was chosen. Results: The determined prescription process contained sofosbuvir (400mg), ledipasvir (90mg), copovidone (97.5mg), croscarmellose sodium (50mg), microcrystalline cellulose (115mg), lactose monohydrate (230mg), magnesium stearate (7.5mg), gum arabic(10mg), opadry film coating powder, and purified water. Conclusion: The determined prescription process was stable and the pesticide effect of prepared tablet was equal to the original tablet, so the prescription design was reasonable.

Key word: Harvoni™, Prescription Technology, Sofosbuvir.

1. Introduction

Harvoni™ was developed by Gilead Sciences, Inc., which is a fixed-dose combination tablet containing sofosbuvir and ledipasvir. Sofosbuvir is a nucleotide analog inhibitor of HCV NS5B polymerase and ledipasvir is an HCV NS5A inhibitor. Each tablet contains 400 mg sofosbuvir and 90 mg ledipasvir^[1-2].

Sofosbuvir was first approved by the United States on December 6, 2013, the IUPAC

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name is (S)-Isopropyl 2-((S)-(((2R, 3R, 4R, 5R)-5-(2, 4-dioxo-3, 4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl) methoxy)-(phenoxy) phosphorylamino) propanoate.

Ledipasvir has not been approved for clinical use alone, and the IUPAC name is Methyl [(2S)-1-((6S)-6-[5-(9,9-difluoro-7-{2-[(1R, 3S, 4S)-2-((2S)-2-[(methoxycarbonyl)amino]-3-ethylbutanoyl]-2-azabicyclo[2.2.1]hept-3-yl]-1*H*-benzimidazol-6-yl]-9*H*-fluoren-2-yl)-1*H*-imidazol-2-yl]-5- azaspiro [2.4] hept-5-yl)-3-methyl-1-oxobutan-2-yl] carbamate.

Harvoni™ was recognized by FDA as a breakthrough therapeutic drug, it is the first fixed-dose combination oral tablet to be preferred approved to treat genotype 1 of hepatitis C without requiring interferon injections. Harvoni™ can be used alone or combine with other oral anti-HCV agents, such as ribavirin.

Currently, the popularity rate of Harvoni™ is very low for its high price, while the number of patients with genotype 1 of hepatitis C is very huge. To meet the needs of patients, increase their choice of medication and reduce the cost of the drug, we should study the combination tablet (Sofosbuvir/Ledipasvir) and make it commercialization, marketization. This not only brings good news to patients, but also can generate enormous social and economic benefits.

2. Reagents and Instruments

2.1 Reagents

Ledipasvir, sofosbuvir, microcrystalline cellulose, croscarmellose sodium, lactose monohydrate, magnesium stearate, copovidone, gum arabic, coating powder.

2.2 Instruments

Laboratory hopper mixer, dry granulator, tablet machine, high efficiency coating machine, high performance liquid chromatography, dissolution tester, electronic balance.

3. Ingredients Screening and Stability Testing

This research was to clone the original drug Harvoni™ (Sofosbuvir/ Ledipasvir). By searching the information on the FDA website, we can know the composition of original drug: croscarmellose sodium, micro sodium cellulose, lactose monohydrate, magnesium stearate, copovidone, gum arabic and coating powder.

The compatibility between excipients and drugs in solid preparations has a very important guiding role in screening prescriptions and process [3]. Through compatibility experiments, we can select the appropriate excipients to ensure the stability of drugs effectively.

According to **Table 1**, the ingredients were mixed with the active ingredient. Placed them under high temperature condition (60 °C), high humidity condition (92.5% RH) and