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Review Article

Drug Optimization: Fighting Research to Achieve the Greatest Use of Darunavir

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Abstract

A design has been development that provides higher activity to darunavir, an antiretroviral drug, aiming a lower dose in the battle against HIV in children and adults. Globally this research paves the way to get a new darunavir: β-cyclodextrin complex driving future perspectives to new anti HIV drugs for clinical applications. β-cyclodextrins not only promote the solubility of darunavir, but can drive to development of new complexes able to combat HIV in lower doses and, therefore lower toxic effects. Analysis methods by chromatography, also, were developed to evaluated the quality of the complexed darunavir. All this effort to contemplate the patients of all ages and provide quality medicines as well as a better quality of life.

Acquired Immunodeficiency Syndrome

Acquired Immunodeficiency Syndrome (AIDS) is the final stage of the disease caused by Human Immunodeficiency Virus (HIV). It attacks the defense cells of the body, leaving the body vulnerable to all kinds of diseases [1-3].

Currently, treatment of HIV infection relies on the called Highly Active Antiretroviral Therapy (HAART) which proposes the combination of several drugs in a daily regimen [1, 4-9].

Therapeutic agents are divided according to their mechanism of action. Darunavir belongs to protease inhibitors such as atazanavir, fosamprenavir, indinavir, lopinavir/ritonavir, ritonavir, saquinavir, tipranavir [1, 10-15].

Darunavir: β-Cyclodextrin

Darunavir, an antiretroviral drug, has low solubility in water and requires administration in high doses [16, 17]. So, it was complexed with β-cyclodextrin [18]. The complex has been studied and compared to free darunavir.

Characterization

Darunavir: β-cyclodextrin complex, by spectrophotometry in the infrared region, shows bands present in the free darunavir and other characteristic bands from complexation [19].

The thermal studies, by thermogravimetry and differential scanning calorimetry with heat flux showed that the darunavir: β-cyclodextrin complex has a higher thermal stability than the free drug and also has characteristic behavior [19].

The darunavir: β-cyclodextrin complex, by X-ray diffraction, shows crystalline form [19].

These techniques can identify darunavir: β-cyclodextrin complex safely and effectively.

Solubility

The solubility of the darunavir: β-cyclodextrin complex was studied and the results were impressive and significant for science and for public health. The darunavir: β-cyclodextrin complex presented solubility 28 times higher than free darunavir in acetate buffer 0.05 M at pH 4.5, 23 times in water purified and 22 times in phosphate buffer 0.2 M at pH 6.8 [16].

This study allows the use of smaller doses of the drug and therefore adverse effects are less frequent. This advantage for patients with AIDS is a great advance, since they are bodies debilitated by the virus and administer many medications daily.

Analytical methods

Method by Thin Layer Chromatography (TLC) and High-Performance Liquid Chromatography (HPLC) were developed for the identification and quantification of darunavir in the darunavir: β-cyclodextrin complex [20, 21]. These methods were also able to identify degradation products of the complex, being considered methods indicative of stability.

The stability of the darunavir: β-cyclodextrin complex was evaluated for 2 years and the results have shown that it is stable at a temperature of 30 °C ± 2 °C and 75 % ± 5 % of humidity [22]. This is another advantage of the complexed darunavir.

Importance

The darunavir: β-cyclodextrin complex can be considered a new technological advance.

The solubility of the complex is 28 times greater than the solubility of free darunavir. This allows the use of smaller doses. Moreover the adverse effects could be decreased by reducing the dosage.

Another aspect to be highlighted is related to its smaller mass which can get smaller pharmaceutical dosage forms.

Children, the elderly or even adults with swallowing problems unable to swallow tablets of 600 mg, such as tablets of darunavir found on the market.

If the dose is smaller, this group of patients can be contemplated by the darunavir: β-cyclodextrin complex.

Patients with the syndrome use many drugs daily and the complex comes to increase the quality of their life, providing fewer side effects, smaller tablets and less taken per day.

This technological advance can improve the life of patients with AIDS and in addition it can help the public health system.

A patient who presents adverse effects of any medication will seek medical attention. A patient who cannot follow pharmacotherapy by confounding medications (many per day) or tablets too big that need to be divided for administration or liquid formulations with bad taste that are administered in amounts wrong or wrongly will seek medical attention. Methods which are not able to properly evaluate the quality of the medications also contributes to the release of pharmaceutical products without quality which will not make its effect and the patient will not be better, even fulfilling pharmacotherapy correctly.

These issues contribute to the vicious circle of medical attention that suffocates the public health system.

Conclusion

The complex was designed to improve the quality of life of patients with AIDS. In this scenario, darunavir: β-cyclodextrin complex contributes positively to society, economy and future of science.

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