Formulation and in-vitro evaluation of extended-release tablet of metformin hydrochloride

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Abstract: Metformin hydrochloride is a biguanide anti-hyperglycemic agent. It is used to manage the type II diabetes (500-3000 mg/day). Extended-release tablets reduce the frequency of dose administration and side effects, meanwhile, the plasma concentration will be constant. As a result, it increases the patient compliance. Furthermore, metformin hydrochloride is freely soluble in water and producing extended-release tablets, which are soluble in the water, is not so easy.

As the main goal, the preparation and evaluation of extended-release tablet of metformin hydrochloride have been investigated.

In order to develop and characterize an oral extended-release matrix tablet of metformin hydrochloride, a combination of cellulose derivatives (HPMC K4M, K10M) and methacrylate derivatives (Eudragit® (RS, S100)) is used. Tablets are prepared by through mixing of the ingredient, followed by wet granulation and direct compression.

All the prepared formulations were evaluated in terms of physicochemical tests, including hardness, friability, weight variation, thickness, assay and in-vitro drug release (for 10h using USP XXXII dissolution apparatus II (paddle) at 37°C and 100rpm in 1000ml phosphate buffer (pH of 6.8)). Furthermore, the kinetic of drug release of the best formula was found and described with zero-order, first-order, Higuchi, Korsmeyer and Hixson-Crowell equations.

Based on the obtained results, the combination of HPMC and Eudragit® RS could efficiently and meaningfully extend the drug release up to 10 hours with suitable profile of drug release.

Notifying that using HPMC and Eudragit® RS separately cannot result in a meaningful drug release extension, their combination with certain concentrations (HPMC by applying two different mechanisms: formation of both gelling structure and erosion of swollen polymer and Eudragit® RS with a complex mixture of diffusion and erosion) is addressed as an effective retardant agent.

Keyword: Metformin hydrochloride, Extended-release, Matrix tablet, Eudragit® (RS, S100), HPMC.