Extended Journal of Biopolymers 2020
Vol.4 Issue.1

Formulation of extended-release gliclazide tablet by using a mathematical model for estimation of Hypromellose

Farzad Khajavi
Research and Development Section, Dr. Abidi Pharmaceutical Company, Iran

Abstract

Formulation of Gliclazide in the form of extended-release tablet in 30 and 60 mg dosage forms was performed using Hypromellose (HPMC K4M) as a retarding agent. Drug-release profiles were investigated in comparison with references Diamicron MR 30 and 60 mg tablets. The effect of size of powder particles, the amount of Hypromellose in formulation, hardness of tablets and also the effect of halving the tablets was investigated on drug release profile. A mathematical model which describes Hypromellose behaviour in initial times of drug release was proposed for estimation of Hypromellose content in modified-release Gliclazide 60 mg tablet. This model is based on erosion of Hypromellose in dissolution media. The model is applicable to describe release profiles of insoluble drugs. Therefore by using dissolved amount of drug in initial times of dissolution and the model, the amount of Hypromellose in formulation can be predictable. The model was used to predict the HPMC K4M content in modified-release Gliclazide 30 mg and extended-release Quetiapine 200mgtablets.

Keywords

Hypromellose, gliclazide, drug release, modified release tablet, mathematical model.

INTRODUCTION

HE reduction of frequency and/or increasing the effectiveness of the drug is the main goal of controlled delivery systems [1]. In these systems, drug release from the dosage form is controlled mainly by the properties of polymer and drug used in the preparations [2]. The commonly used polymers for controlled release are hydroxypropylmethylcellulose or hypromellose (HPMC), hydroxypropylcellulose (HPC), hydroxyethylcellulose (HEC), ethylcellulose (EC), methylcellulose (MC), carboxymethylcellulose (CMC), polyvinylpyrrolidone (PVP) and polyethylene glycol (PEG). These polymers, which swell in aqueous medium, are often used for the preparation of controlled release dosage forms. These are highlighted with the presence of a solvent front, the potential for unlimited swelling, and the combined controlling mechanism of diffusion and erosion as being the distinguishing feature of HMdevices [1]. Cellulose ethers are found to accommodate a large percentage of drugs and are easy to use in tablets. They are also very stable over a wide range of conditions. In the presence of strong acid, water, and heat, a cellulose ether polymer will be degraded by chain scission causing a loss of average molecular weight or viscosity. HPMC is often used to prepare matrix of sustain release (SR) tablets because the polymer is non-toxic and easy-to-handle and it does not require any special manufacturing technology [3]-[6]. It was evident that HPMC 2208 (methocel K4M premium) and carboxy vinyl polymers can release drugs for longer time by quickly forming a gel layer [1]. Tahara et al. described overall mechanism behind matrix SR tablets prepared with hydroxypropyl methylcellulose 2910 [7]. Many factors affecting the release of drugs from cellulose matrices have been investigated [8]. The particle size of polymer is a key parameter because it affects hydration rate and thus the rate of gel formation and drug release. Another important factor isviscosity of the polymers, which is higher as the molecular weight increases. If the viscosity of the polymer increases, the gel layer viscosity also increases, so that the gel layer becomes resistant to dilution and erosion [1]. The drug release rate is then slower. Like viscosity of the polymer, the concentration of polymer can also affect the strength of the gel. The increase in polymer concentration can result in stronger diffusion layer that is resistant to diffusion or erosion. Ultimately, this will slow drug release [1]. Size and shape (e.g. tablet or capsule) of matrix are the other factors. For instance, smaller tablets will generally require higher polymer content. An increase in tablet size can result in slower drug release due to a smaller surface to volume ratio and a smaller amount of initial gel formation [1]. In this work, we investigate whether making smaller particles of ready-to-press powder of modified-release gliclazide tablets can have an impact on drug release profile; the effect of hardness was investigated on drug release, also the drug release profile of half of a tablet of modified-release gliclazide 60 mg was investigated and compared with modified-release gliclazide 30 mg tablet and Diamicron MR 60 mg tablet as a reference tablet. The mathematical model was developed to investigate the behaviour of HPMC in initial times of drug release profile of modified-release gliclazide 60 mg tablet. Estimation of HPMC amount in formulation will be feasible through the data of dissolved amount of drug in initial times and the proposed model. This model will give us a good estimation of HMPC amount in formulation and will reduce the experiments to optimize the content of HPMC in modified-release gliclazide tablets. Also, this model can be used in other formulations to predict HPMC amount. It was used to predict HPMC amount in extended-release quetiapine tablets and good estimation was achieved by the model.

RESULTS AND DISCUSSION

After making of modified-release gliclazide 30 mg granule (internal phase), the dried granule was passed through the oscillating granulator with 16-mesh screen and mixed with the remaining of excipients (external phase). Then, the compression was completed (HPMC content was considered 20% informulation). The sixmodified- release tablets with an average hardness of 7.1 kp (kilopond) were selected for in vitro test study. Six tablets of Diamicron MR 30 were used as reference tablets. The dissolved amount of gliclazide tablet in dissolution medium was obtained at time intervals of 1h, 2h, 4h, 8h, 12h, and 16h using an appropriate calibration curve for gliclazide. Dissolution profiles of gliclazide and Diamicrontablets werecompared
using a similarity factor equation (2) and difference factor equation (1).

Email: farzadchemistry@gmail.com

This work is partly presented at Joint Event on International Conference on Polymer Waste-Biopolymers & Bioplastics, October23- 25, 2019 at Frankfurt, Germany