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Stirring Speed Effects on Physical Characteristics of Theophylline Microsphere

Gülen Melike Demir,Alptuğ Karaküçük, Zelihagül Değim
Gazi University/Faculty of Pharmacy/Department of Pharmaceutical Technology
06330/Ankara/Turkey

Derya Bektaş
Derya Bektaş Pharmacy, 06790, Ankara, Turkey

Özlem Çoban
İlko-ARGEM, Research and Development Department, Ankara, Turkey

Ezgi Gülpınar
Ezgi Gulpinar Pharmacy, 06620, Ankara, Turkey

Sema Tuna Torunoğlu
Çubuk Park Pharmacy, 06760, Ankara, Turkey

Extended Abstract

Microspheres (MS) are small spherical particles, with different diameters in the micrometer range (typically 1 μm to 1000 μm) (Kaur JK et al. 2003). Microspheres are generally biocompatible, can provide high bioavailability, and are capable of sustained release for long periods of time. Theophylline is a methylxanthine alkaloid that is used in the treatment of asthma as a bronchiodilator. Theophylline has a narrow therapeutic index in the range of 5–20mg/ml (Obeidat WM et al. 2006).

Microsphere characteristics are greatly affected by processing and formulation variables such as stirring speed, drug solubility, solvent type, temperature, morphology and drug loading have been reported frequently. Clearly, microsphere size will strongly affect the rate of drug release by acting rate of drug diffusion (Obeidat WM et al. 2006 and Berklanda C et al. 2004).

The objective of this investigation was to evaluate the effect of stirring speed on particle size. In this study, Eudragit RS 100 that is a copolymer of ethyl acrylate, methyl methacrylate and a low content of methacrylic acid ester with quaternary ammonium groups were used as a polymer and polyvinyl alcohol (PVA) was used to reduce the surface tension. Microspheres containing theophylline were prepared by the emulsion-solvent evoporation method. First, polyvinyl alcohol solution at concentration of 0.4% (w/w) was prepared dissolving in distilled water. Theophylline solution in distilled water was added to the polyvinyl alcohol solution under magnetic stirring. Finally, Eudragit RS 100 solution in dichloromethane was added to PVA-Theopylline solution under ultra-turrox. The adjustment was based on the use of stirrer in different stirring speeds (as 8000 rpm, 13500 rpm, and 20000 rpm), thus reducing the size of MS. Thereafter, the size reduction process resulted in the micrometer range.

Three different stirring rates (8000, 13500 and 20000 rpm) were investigated. Particle size measured as 72,54μm; 34,81μm and 13,67μm at three different stirring rates (8000, 13500 and 20000 rpm, respectively). Zeta potentials were measured to be -0,149, -0,135 and 0,245 mV for three samples at different speed rate 8000, 13500 and 20000 rpm, respectively. Zeta potential increased with rising stirring speed correspondingly. Furthermore, the polymer surface on the microsphere is larger when the microsphere size is bigger and the particle shape is observed homogeneous and spherical in all formulation.

The particle size decrease depends on escalating speed (Heiskanen H et al. 2012). In accordance with our study results too, the particle size decreased with increasing rotating speed. Moreover, smaller particle size produced greater surface area and zeta potential changed to positive. As a conclusion, the sample stirred at 20000 rpm is more stabile and the best fitting candidate.

References

Heiskanen H, Denifl P, Pitkänen P, Hurme M, Effect of preparation conditions on the properties of microspheres prepared using an emulsion-solvent extraction process, Chemical Engineering Research and Design,90,1517–1526,2012.

Kaur JK, Tambwekar K, Garg S. Bioadhesive microspheres as a controlled drug delivery system. Int J Pharmaceut.255,13–32,2003.

Obeidat WM, Price JC. Preparation and evaluation of Eudragit-S100 microspheres as pH-sensitive release preparations for prioxicam and theophylline using the emulsion-solvent evaporation method. J.Microencap.23(2),195-202,2006.

Berklanda C, Kipperb MJ, Narasimhanb B, Kimc K, Pack DW. Microsphere size, precipitation kinetics and drug distribution control drug release from biodegradable polyanhydride microspheres. J Cont. Rel. 94,129–141,2004