

Controlled drug release of methylphenidate through pelletization process

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Background and Aims: Methylphenidate (MPH), a mild psychostimulant drug administered orally in ADHD, narcolepsy and postural orthostatic tachycardia syndrome has a short 2-4 hours half life and 3-5 hours duration of action. Thus, frequent MPH administration is required to maintain its therapeutic blood level. The main objective of the present study was to utilize simple pelletization technique to prepare MPH pellets suitable for the once daily dosing schedule.

Methods: MPH matrix pellets consisting Avicel, lactose, magnesium stearate and different amounts of GMS, Eudragits (RSPO, RLPO, RS30D, and RL30D), carbomer, HPMC and Na CMC were prepared by extrusion-spheronization technique. The particle size of the pellets was determined by the sieve analysis. Hardness, weight variation and disintegration time of pellets were also evaluated. The drug dissolution study was carried out in 900 ml water at 37°C using USP apparatus (paddle) at 50 rpm for 12 hours. The content uniformity of pellets was also determined according to the USP guidelines.

Results: Most 28 pellet formulations had acceptable physical properties with regard to size distribution, sphericity, flowability, crushing strength and friability. MPH pellets comprising Avicel 60%, Eudragit RSPO & RLPO 5%, GMS 15% and HPMC-K15M 15% were, however, released the drug in a more time-controlled manner than other formulations with the release of 50%, 60% and 70% of its drug content after 60, 210 and 420 min, respectively. Hardness and pellet size did not have significant effects on drug release from pellets.

Conclusions: Simple pelletization can be used to produce MPH pellets exhibiting a dual release pattern of a burst release followed by a slower release rate, providing the loading and maintaining doses of drug. This can benefit patients with avoiding repeated dose administration and improve their compliance.

Keywords: Methylphenidate; Pellet; Dual release pattern; Sustained release