An Overview of Factors affecting Superdisintegrants Functionalities

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ABSTRACT

Disintegrants are an essential excipients in solid oral formulations. Superdisintegrants such as croscarmellose sodium, sodium starch glycolate, crospovidone and polacrilin potassium are among excipients added in immediate release and oral dispersible tablet formulations at low concentrations to counteract effects of compression and binder after administration. Hygroscopicity of superdisintegrants facilitates permeation of water into tablet matrix and cross-linkage reduces their solubility in water. This article describes factors which could affect functionality of superdisintegrants such as molecular and physicochemical factors (degree of cross-linkage and substitution, particle size, particle porosity and impurities); formulation and process factors (solubility and hygroscopicity of fillers and/or binders, incompatibility, pH, lubricants, mode of disintegrant addition, granulation, mixer shear rate, compression pressure and reworking) and aging and storage conditions.

KEYWORDS: Superdisintegrant; Sodium starch glycolate; Croscarmellose sodium; Crospovidone; Polacrilin potassium; Disintegration, dissolution.

Introduction

Disintegrants are one of tablet excipients added to eliminate cohesive strengths introduced by compression and binders (Kottke and Rudnic, 2002). Disintegrants facilitate permeation of water into tablet matrix, thereby the tablet changes into coarse aggregates and the coarse aggregates in turn deaggregate into primary particles (Desai et al., 2016). The formation of smaller particles increases the surface area of drug available for physiological medium, hence enhanced dissolution rate and bioavailability of the drug (Quodbach and Kleinebudde, 2016).

The term ‘superdisintegrant’ was came into use at the end of 1970s or beginning of 1980s to describe the then new generation of disintegrants that were much more effective at low concentration compared to conventional disintegrants (Moreton, 2008). Being effective at low concentrations, superdisintegrants give economic advantage as well as reduce flow and compression problems related with the use of relatively higher proportions of starch (Van Kamp et al., 1983).

Superdisintegrants include sodium starch glycolate (SSG), croscarmellose sodium (CCS), crospovidone (XPVP) and polacrilin potassium (PP) (Quodbach and Kleinebudde, 2016). They are very hygroscopic because they contain polar functional groups. The presence of cross-links in their polymer structure minimizes conformational degrees of freedom, as the result the polymer matrix behaves highly resistant to gelation and dissolution (Barmpalexis et al., 2018). They are commonly used in immediate release and oral dispersible tablet formulations at low concentration levels.

Recently excellent review works have been done on different subjects of disintegrants (Zarmpi et al., 2017; Markl and Zeitler, 2017; Desai et al., 2016; Quodbach and Kleinebudde, 2016). However, the emphasis given in these works about factors affecting performances of superdisintegrants is not adequate. Thus, this article provides an overview of key factors affecting performances of superdisintegrants in solid oral pharmaceuticals.

Sodium Starch Glycolate (SSG)

SSG (Fig. 1) is carboxymethyl ether substituted and phosphate ester cross-linked superdisintegrant produced typically from potato starch (Bolhuis et al., 1986; Quodbach and Kleinebudde, 2016). Carboxymethylation is performed as Williamson ether synthesis, i.e., starch is made to react with sodium chloroacetate in alkaline medium and then neutralized with citric acid or other acids. Cross-linking is performed using chemical or physical methods. In chemical method, reagents such as phosphorous oxytrichloride, sodium trimetaphosphate or other cross-linking reagents are used (Bolhuis et al., 1986). Carboxymethyl group makes SSG to have

ABBREVIATIONS: DT = disintegration time; SSG = sodium starch glycolate; CCS = Croscarmellose sodium; XPVP = crospovidone; PP= polacrilin potassium