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Short communication

Impact of disintegrant and lubricant on disintegration and dissolution of immediate-release tablets

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Introduction

Formulating BCS Class II active pharmaceutical ingredients (low solubility, high permeability) is challenging, as dissolution is the rate-limiting step for absorption (Amidon et al., 1995). The investigated API is formulated as a bisulfate salt to improve aqueous solubility in acidic environments (Aulton et al., 2013), though its susceptibility to hydrolytic degradation requires careful excipient selection to maintain stability.

Disintegrant and lubricant selection significantly influences direct-compression tablet manufacture. Crospovidone acts mainly through capillary water uptake and particle shape recovery, while croscarmellose sodium promotes disintegration primarily through swelling and water uptake (Berkenkemper et al., 2020; Rowe et al., 2012). Talc, hydrogenated castor oil (HCO), and stearic acid are hydrophobic excipients that may reduce wettability and delay disintegration/dissolution, whereas sodium stearyl fumarate (SSF) and polyethylene glycol 6000 (PEG 6000), being more hydrophilic, generally have less negative impact on dissolution (Rowe et al., 2012). This study investigated the influence of different disintegrants and lubricant systems on disintegration, dissolution, and hardness of immediate-release tablets prepared by direct compression.

Materials and Methods

Five formulations (F1–F5) were prepared using mannitol (diluent), microcrystalline cellulose (binder), colloidal silicon dioxide (glidant), crospovidone and croscarmellose sodium (superdisintegrants), and talc, stearic acid, HCO, PEG 6000, and SSF (lubricants). The API and other ingredients, except lubricants, were weighed, sieved, and blended to homogeneity; lubricants were then added and blended for 1 min at low speed.

F1 contained no disintegrant, with talc (6%) and stearic acid (4%). F2 contained crospovidone (5%), and F3 contained croscarmellose sodium (5%); in both, the lubricants were the same as in F1. F4 contained crospovidone (5%), talc (3%), PEG 6000 (3%), and HCO (1.37%). F5 contained crospovidone (5%), talc (3%), and SSF (1.5%).

Bulk/tapped density, powder flow (Carr's Index, Hausner Ratio), hardness (N), disintegration time (min), and dissolution were determined according to the European Pharmacopoeia (2023).

Results and Discussion

Acceptance criteria were set as disintegration ≤ 15 min, dissolution ≥ 80% within 30 min in 0.1 N HCl, hardness 50–80 N, and assay 95–105% of declared dose (European Pharmacopoeia, 2023; FDA, 2017).

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All five formulations demonstrated acceptable powder flow (Carr's Index < 15%, Hausner Ratio < 1.18), confirming suitability for direct compression (European Pharmacopoeia, 2023).

Effect of disintegrants and lubricants on disintegration and dissolution

Formulation 1 (no disintegrant) showed the longest disintegration time (> 17 min) and lowest dissolution (51.19%), confirming that disintegrant absence substantially compromises drug release from BCS Class II formulations (Aulton et al., 2013). Among the superdisintegrants, both improved performance over Formulation 1, with crospovidone (F2: < 9 min, 91.12%) achieving higher dissolution than croscarmellose sodium (F3: < 6 min, 86.18%), attributed to its pH-independent capillary action, multi-mechanism action and lower tendency for gel layer formation, which may transiently slow drug release in BCS Class II formulations (Berkenkemper et al., 2020; Bauhuber et al., 2021).

Regarding lubricant effects, Formulation 4 (talc 3%, PEG 6000 3%, HCO 1.37%) showed the highest dissolution (98.89%, < 9 min), suggesting that PEG 6000 further enhanced matrix wettability. Formulation 5 (talc 3%, SSF 1.5%) showed disintegration < 7 min and dissolution of 96.74%, indicating that reduced hydrophobic lubricant content may improves water penetration. A direct comparison of talc concentration alone is limited by simultaneous changes in lubricant type across formulations.

Effect of formulation composition on hardness

Tablet hardness was influenced by disintegrant and lubricant type. F1-F3 (talc 6%) showed higher hardness (64-82 N), indicating a more compact structure (Lieberman et al., 2008), while F4 (talc 3%, PEG 6000, HCO) and F5 (talc 3%, SSF) showed lower hardness (50-65 N and 52-58 N, respectively), likely due to increased plasticity and reduced interparticle bonding (Aulton et al., 2013). All formulations met the target hardness range; F4's reduced hardness did not affect performance, showing rapid disintegration and superior dissolution (Lieberman et al., 2008).

Conclusion

The results demonstrated that both disintegrant type and lubricant composition significantly influence the disintegration and dissolution of immediate-release tablets containing a BCS Class II API. The absence of a disintegrant resulted in insufficient dissolution, confirming its essential role in drug release. Among the superdisintegrants evaluated, in F2 higher dissolution, compared to F3, attributed to its multi-mechanism disintegration action and lower gel-forming tendency. Regarding lubricants, formulations with reduced hydrophobic lubricant content and incorporation of more hydrophilic alternatives (F4, F5) showed improved dissolution (98.89% and 96.74%, respectively), indicating enhanced tablet wettability. All optimised formulations met the predefined acceptance criteria for disintegration, dissolution, and hardness, supporting their suitability for further development.

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