EVALUATION OF CHITIN METAL SILICATE CO PRECIPITATES AS POTENTIAL MULTIFUNCTIONAL EXCIPIENTS IN TABLET FORMULATIONS

By

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Abstract

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Under the supervision of Prof. Mohammed Shubair and Dr. Faisal Al- Akayleh

Three novel chitin metal silicates (CMS) were prepared namely chitin calcium silicate (CCaS), chitin magnesium silicate (CMgS), and chitin aluminum silicate (CAlS).

These CMS were tested as multifunctional direct compression and wet-granulation excipients in the design of tablets containing ibuprofen (IBU), metronidazole (MET) and spironolactone (SPL) as models of low and high dose drugs.

Commercial tablets containing these drugs and tablets made using Avicel® 200; one of the most commonly and widely used commercial direct compression excipient; were studied for comparison purposes.

The pH of the media of preparation of these CMS co precipitates was measured to be: 10, 9, and 4 for CCaS, CMgS, and CAlS, respectively. CAlS was selected to test the effect of altering this pH from 4 to 7 or 8 and found to highly

affect its functionality with respect to hardness, disintegration time and dissolution rate.

The friability values for all the prepared tablets were below the maximum 1% USP tolerance limit. All CMS containing formulas showed crushing strength within the acceptable range (>40N). For all tested drugs, the CMS (prepared at their appropriate $pH_{(s)}$, 10, 9 and 4 for CCaS, CMgS and CAlS respectively) based tablets showed outstanding disintegration characteristics (disintegration time less than 60s) for tablets prepared by direct compression or wet granulation methods. The type of CMS was found not to affect the disintegration time and crushing strength of the tablets. Regarding the dissolution profiles, CMS tablets demonstrate superiority over the Avicel® 200 based tablets except for those with metronidazole which showed similar dissolution profile. In addition, they demonstrate faster dissolution profiles than Fleximex® and Dumazole® but slower than Aldactone®.

Compressional properties of formulations were analyzed using density measurements and the compression equations of Heckel and Kawakita as assessment parameters. CMgS was selected as an example. All tested formulas gave plots with an initial curved region followed by a linear portion, which is typical of B-type materials; this indicates that the materials first underwent fragmentation, followed by plastic deformation. Formulas containing CMgS with ibuprofen, metronidazole or spironolactone showed lower yield values (Py) than CMgS alone which indicate faster onset and higher amount of plastic deformation. A linear relationship was found to exist between P/C (applied pressure/degree of volume reduction) and P (pressure) for all tested formulations (CMgS alone and CMgS with ibuprofen, metronidazole or spironolactone). The value of “1/b”; which represents the cohesive properties of powders, for CMgS alone is higher than those with drugs. The lower value of “1/b” of

CMgS in the presence of drugs is indicative of the reduction in cohesive forces. In other words, the presence of drugs increased the plastic deformation of CMgS under pressure. These results are in positive correlation with Heckel parameter (Py).

Differential scanning calorimetry (DSC) was used as a screening technique for assessing the compatibility of the model drugs with CMS employed in tablet formulations. On the basis of DSC results, CMS co precipitates were found to be chemically compatible with the tested drugs.

These results conclusively show that the prepared CMS co precipitates have the potential to be used as filler, binder, and disintegrant, all-in-one, in the design of tablets containing either a low or high dose drug by direct compression and wet-granulation methods.

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