Study of the Tableting Properties of MCR, a Newly Coprocessed Cellulose-based Direct Compression Excipient

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The current need for strategies to accelerate and optimize the efforts to develop new in-expensive multifunctional direct compression tableting excipients with minimum risk to the products has urged the workers in pharmaceutical industry field to search for a simple and low cost-effective technique to tailor and engineer multi-functional excipients. Developing new pharmaceutically inactive materials serving as excipients, new grades of existing excipients and co-processing of already existing excipients constitute the techniques utilized to develop multi-functional excipients [1-3]. Developing of new tableting excipients is a tedious and time consuming multi-stage process. In addition to that, the regulatory concerns and issues related to safety and toxicity assessment should be strictly followed. The co-processed excipients can be at high cost effective. Therefore, a great deal of attention was directed to co-processing as a means to develop multifunctional excipients [4-7]. This technique has been defined as particle engineering of individual excipients and excipient combinations using co-processing by virtue, of sub-particle modifications [4,5]. The workers in pharmaceutical industry field has accelerated the steps towards developing direct compression tableting excipients of high functionality in terms of flow, compression, good binding, improved lubricating efficiency and improved dilution potential could be developed [5-8]. Co-processed excipients are produced from two or more existing excipients of different chemical nature. Each excipient exerts a special function in formulations as well as in the corresponding tablets. It should be clear in mind that the physico-chemical properties of the co-processed excipient is, to a great extent, affected by the chemical nature of the excipients contributed to co-processing.

One of these trials resulted in introducing (MCR) [9] which was co-processed with varying portions of locally extracted microcrystalline cellulose (CMCC) and its corresponding regenerated cellulose (CRC). Engineering of particle size as well as simple mixing and granulation by slugging techniques were employed in co-processing. Two particulate systems were involved in co-processing: First is comprised of amorphous, large (effective mean diameter is 90 µm), elongated, fibrous intermeshing, aggregating and non-freely flowing particles. The second is comprised of nearly fine (effective mean diameter is = 3 µm), spherical, non-aggregating, and freely flowing particles. Employing such particulate systems to co-process excipients lessen the inter-particle friction and the resistance against flow created as a result of the intermeshing of the large fibrous particles during flow. Moreover, the adsorbed fine particles onto the surface of the elongated fibrous particles create isolating layer film which facilitates particles slippage during flow and decreases the inter-particulate friction and the friction between particles and the wall of the container and pipes of the compression machine. Therefore, MCR showed reduced repose angle (38 degree) and high value of Hauser’s ratio which are more or less favorable to free flowing powders. The flow rate measured for MCR powder was high (1.2 gs⁻¹). This result reveals that MCR copes with tableting machinery’s increasing speed capabilities, which require excipients to maintain good flowability and low weight variation even at short dwell times. MCR followed by CRC produced more uniform tablets. The high, steady, and continuous flow of MCR powder upon compression gave rise to uniform tablets.

Employing excipient of a large surface (where bonding sites, α, are available) such as CRC in co-processing leads to develop excipients of improved compression and compaction properties. MCR showed higher values of
Compressibility, $k_{\varepsilon}(-0.2)$, and compactibility, $k_{\kappa}(0.69)$, indexes, respectively. MCR produced tablets of higher crushing strength and lower friability levels. Usually, the energy consumption (or work done) during compression is calculated from the area under force-displacement curve, (AUC). More compressible excipients generate larger AUC value. In case of compressing tablets from a confined concentration, $C$, of MCR under fixed machine settings, $\alpha$ in the used MCR is considered the predominant working parameter concerning the energy consumed for bonding the particles together and holding the structure of the tablet body. The energy consumed for bonding the particles was calculated from the plot of $C$ of the excipient used to compress tablets vs the reduction in the height of the compressed tablets. MCR generated larger AUC value ($\approx 2.3 \text{ cm}^2 \times 10^{-2}$).

Although CRC has the largest surface area, it generated low $k_{\varepsilon}$ and $k_{\kappa}$ indexes and small percent compressibility value. This is because it has reduced ductility [10]. The reduced ductility of CRC may be due to the physical modification of the molecules taken place under the effect of the alkali metal used in processing. On the other hand, the high moisture content of CRC (6.4% w/w) may negatively affect its compression characters. This is why CRC failed singly to produce satisfactory tablets. The compression characters of CRC could be improved by co-processing with a ductile component which is, in this instance, CMCC and produced MCR which is more compressible and suitable for producing satisfactory tablets.

The large surface area, large hydration capacity, and large swelling index of MCR all reveal that it has high disintegration and hence high dissolution functionalities.

$\alpha$ which is the keyword to understand the tableting functionalities of MCR, was calculated from:

$$\alpha = L_k wt. \Sigma(r_i/MW_i)$$  \hspace{1cm} \text{Eq.1}$$

where $L_k$, wt., $r_i$, and MW, stand for Avogadro’s number $(6.022 \times 10^{23})$, the weight of the MCR in the tablet batch, the fraction of a parent excipient used in co-processing, and its molecular weight, respectively.

**Conclusion**

MCR, a multifunctional cellulose based excipient was successfully co-processed by controlling particle size and size distribution of locally processed micro-crystalline cellulose, CMCC. CMCC and CRC (the corresponding less compressible regenerated cellulose or cellulose II). CMCC and CRC were employed as parent components for co-processing. MCR was freely flowing and highly compressible multifunction tableting excipient. Direct compression tablets of enhanced mechanical properties (crushing strength, porosity and friability) were directly compressed from MCR.

MCR also showed powerful disintegration properties. It possessed high disintegration activity. Tablets compressed with MCR are expected to dissolve within short times. The mechanical properties as well as the disintegration activity of MCR powder were functions of the number of bonding sites $\alpha$ available on the surface of the powder and participating actively in bonding under compression.

MCR was unfortunately sensitive to magnesium stearate the commonly used tablet lubricant. In other words, co-processing failed to overcome the sensitivity of cellulose excipients against magnesium stearate.

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