

The history of the disintegrant concentration biology essay

[Science](#), [Biology](#)



Disintegrant concentration

The production of each batch for the testing concentration value began by the mixing of the powder using the doubling up method in a mortar and pestle, the doubling up method ensured the production of a homogenous mixture. The tablets were then compressed to form a solid tablet with a smooth surface and no visible imperfections. The effect disintegrant concentration has on powder flow properties was clear to see by the appearance and consistency of the powder, at the lower concentration ranges a large amount of aggregation was observed which decreased as the concentration increased. Each batch of powder that was produced underwent testing to find more information about their characteristics regarding flowability and compressibility. The findings of these tests are shown in the table 5. 1 below:

Concentration (% w/w)	Bulk density	Tapped density	Hauser ratio	Carr's index (%)
10	0.460	0.681	1.463	1.4820
20	0.450	0.641	1.422	1.7350
30	0.460	0.641	1.412	1.0910
40	0.660	0.831	1.272	1.05

Table 5. 1. Results of powder characteristics studies for powders produced containing different concentrations of MCC (1-10% w/w)

The results for the powder characteristic studies showed that many of the powders had values, for the Hauser ratio and Carr's index, above 1.25 and above 25 respectively both of which indicates poor flow properties (as shown in table 4. 1. These values give an indication of the uniformity of the powder flow during the die filling stage and it will also indicate how the powder will react when subjected to compressive forces during the tableting process. The reliability of the Carr's index and the Hauser ratio was supported by the appearance of the powder where the disintegrant concentrations were in the lower concentration ranges, these powder showed a large amount of aggregation, showcasing

properties similar to mannitol, which also showed poor flow properties and had a greater tendency to aggregate into lumps than the MCC. At 5% and above the powder shows less of a tendency to aggregate showcasing flow properties somewhere in between mannitol and MCC, however as shown by the results in table 5. 1 the flowability of the powder did not vastly improve. The greatest improvement in flowability and compressibility is seen at the 10% concentration range where the Carr's index falls below 25 and the Hausner ratio is just above 1.25, the powder was also more free flowing than all other batches and did not aggregate at all, the properties of the mixture were more akin to that shown by the MCC which in itself was very free flowing. The effect the concentration of disintegrant has on the flowability/compressibility of the mixture is shown by Olayemi et al (2010) who also found that as the concentration of MCC increased the Carr's index decreased, showing an improvement in flow properties and compactibility as concentration increased. It has also been noted that some polyols (such as mannitol) act as filler/binders and mannitol especially is noted to have caused adhesion problems when present in high concentration due to the needle-like structure of the crystals (Bolhuis, Rexwinkel and Zuurman, 2009). Once the results of the characteristic studies had been collected 30 500mg tablets were formed and tested, the results of which can be seen below.

Concentration (% w/w)	Weight (g)	Thickness (mm)	Diameter (mm)	Hardness (N)	Friability (%)	Disintegration time (s)
10.5 ± 0.01	2.9 ± 0.10	13.0 ± 0.03	12.9 ± 0.05	13.0 ± 0.03	12.9 ± 0.05	13.0 ± 0.03
03125.6 ± 36.33	3.41 ± 0.12	123.6 ± 7.83	20.5 ± 0.03	2.8 ± 0.05	13.0 ± 0.03	13.0 ± 0.03
04115.4 ± 18.34	0.88 ± 0.06	1.6 ± 0.09	6.95 ± 0.01	2.7 ± 0.03	13.0 ± 0.03	12.9 ± 0.05
4 ± 21.57	1.04 ± 0.04	2.71 ± 0.06	10.5 ± 0.01	2.7 ± 0.04	13.0 ± 0.03	36.2 ± 10.03

412. 1418 ± 2.12 Table 5. 2. Results of tablet testing for tablets produced containing different concentrations of MCC (1-10% w/w) with each result being displayed as mean \pm SD (except friability) Once ANOVA was performed on the data collected from the experiment there was no significant difference between groups for the weight and diameter ($p > 0.05$) was found however for thickness, hardness and disintegration time $p < 0.05$ so there is a significant difference between the concentrations. There is a large degree of variation between the disintegration times between the different powder concentrations, with 10% w/w showing the shortest disintegration time with the 1% w/w showing the longest time. The structure of MCC molecule aids the rapid disintegration of the tablet; the crystallites are bonded to each other by weak hydrogen bonds which are easily broken when in the presence of water, causing the production of pores in the tablet and smaller crystallites to break away. These pores allow the entry of more water into the molecule causing other MCC molecules to break leading to the loss of the structure of the tablet. As well as forming pores, the MCC also swells by absorbing the water causing a breakdown of the tablet structure (Sarymsakov et al, 2002). The reason for the variation between the values could be due to the difference in the distribution of the superdisintegrant in the tablet and the influence this has due to the way MCC works as a disintegrant, as there is more disintegrant available in the 10% tablet the water will come in contact with the MCC faster and have more of an effect than at 1% causing the difference in disintegration time. The next value that was varied between the groups was the difference in hardness between the tablets. The values seen vary by more than 60N between the highest and

lowest values. The difference in hardness may be due to the difference in the amount of filler present in the mixture. At higher concentrations mannitol exhibits binder properties (Ghosh and Jasti, 2010). The improvement in the hardness value of the tablets is could be due the production of strong hydrogen bonding formed due to the close proximity of the molecules to each other, each mannitol molecule has 6 hydrogen bond acceptors and donors which provides many points where bonding can occur between molecules causing an increase in tablet hardness. The final significant difference between the concentrations was the tablet thickness. The thickness decreased as the concentration of disintegrant increased, this value can be linked the results seen in the table 5. 1 for powder characteristic studies, the results of the study showed a improvement in the value for the compressibility index (Carr's index) as the concentration value increases. As shown by table 4. 1 in the method section the lower the value the better the flow properties leading to more uniform die filling and better compaction of the powder. The improvement in compactibility can be due to properties shown by MCC such as undergoing plastic deformation and the mechanical interlocking between particles during the direct compression process (Nyström, Alderborn, Duberg,& Karehill, 1993) please wait paper. Talk about wrong result for friability and hardnessFrom the results in tables 5. 1 and 5. 2 it was decided that the 2 most likely candidates capable of producing ODT's capable of passing further testing were the tablets at concentration values of 5% and 10%. Both tablets had low disintegration times and showed uniformity for the results for tablet thickness, width and diameter however at 10% the values for tablet hardness were very low when

compared to the other results, also the tablets produced also showed a loss of 2.14% in weight on the testing of the friability of the tablet. The tablets produced using the 5% powder mixture showed acceptable values for a vast majority of the experiments while having the second lowest loss on friability testing and the second fastest disintegration time of any of the tablets produced, that is why for all future testing the 5% w/w powder mixture was used.

Compression force The term Compression refers to a reduction in the bulk volume of materials as a result of displacement of the gaseous phase, by changing the compressive force used it is thought that the amount of gaseous phase displaced changes accordingly. Once testing of the concentration ranges of disintegrants was completed and the ideal value was found it was then used in the next part of the research, the testing to find the ideal compression force for the production of ODT's. The results of testing are shown in table 5.

Compression force (tons)	Weight (g)	Thickness (mm)	Diameter (mm)	Hardness (N)	Friability (%)	Disintegration time (s)
10.49 ± 0.01	3.0 ± 0.04	13.0 ± 0.01	7.2 ± 11.68	1.62	36.4 ± 1.67	20.5 ± 0.01
12.7 ± 0.03	3.0 ± 0.03	12.9 ± 0.03	29.4 ± 21.57	1.10	40.4 ± 6.27	50.51 ± 0.01
12.7 ± 0.03	3.0 ± 0.01	20.0 ± 9.98	0.89	153.4 ± 5.90	70.51 ± 0.01	12.7 ± 0.06
13.0 ± 0.02	213.4 ± 11.00	1.77	317.8 ± 25.33	Table 5. 2. Results of tablet testing for tablets produced using a range of compressive forces (1-7 tons) with each result being displayed as mean ± SD (except friability)		

Following the analysis of the data it was found that there were significant differences between the group for the weight, thickness, hardness and disintegration time ($p < 0.05$). The lack of difference between the groups for the diameter can be attributed to the fact that the same powder

was used production of the tablets so die was filled uniformly. The difference in weight can be attributed to compression force used. Powder Compression is defined as the reduction in the volume of a powder bed in a confined space caused by the application of a force, so it is the displacement of air between the powder particles which causes the production of interparticle bonds. The strength of the bonds determines the appearance of the tablets and also influences the presence of imperfections on the tablet. At 1 ton of pressure the interparticle bonds have not fully formed causing imperfections to be present on the tablet such as small bits of the tablets breaking off on the removing of the tablet leaving chips in the tablet. This can be seen in figure 5. 1 where imperfections can be clearly seen where the edge of several tablets have broken off and the tablet face on a tablet is not as smooth as it should be. The loss of fragments from the tablets may have caused the difference in weight of the 1 ton of pressure when compared to the other tablets. Once the p value is recalculated by taking out the results for 1 ton compressive force it increases to 0. 33 which means there is no significant difference between the groups. C:

UsersGaganDesktopDocumentsPictures20130220_144402. jpgFigure 5. 1. Tablets produced using 1 ton pressure, imperfection can be seen such as chipping of the tablet or uneven tablet faceThe difference seen between the tablets for thickness, disintegration time and hardness can also be explained by the strength of the interparticular bonds and the amount of air present between particles due to the compressive force put on the powder bed. The effect compression force has on disintegration time is also clearly visible, as the compression force increases the disintegration time increases. The

increase in tablet density, caused by the increase in compression force, reduces the amount of liquid that is able to penetrate the tablet which prevents the contact of between disintegrant and liquid required for tablet disintegration (Marais et al, 2003) which caused the increase in disintegration time. The tablet batches in which all of the disintegration times were within acceptable values were the tablets produced with 1 and 2 tons of pressure, this result is in line with research done by Pabari and Ramtoola (2012) who tested the optimum tablet size and compression force required for ODT's, they found that 15 kN (1.5 tons) of pressure produces a tablet with a disintegration time of 37.1 s Which is well within European pharmacopeia value of a disintegration time of 3 min (180s). Finally the hardness of the tablets was noted to have increased on the changing of the compressive force, as stated earlier the application of force pushes the air out of the powder bed and causes the production of interparticle bonds, at higher compressive forces the bonds formed are very strong causing the increase in tablet hardness seen. At 7 tons of pressure the tablets were well formed with no visible imperfections and produced excellent results for hardness as expected however they were brittle, on removing from collecting tray after friability testing it was noted that several tablets had shattered producing small fragments which has resulted in the loss on friability testing of 1.77%. From the results shown in table 5.3 and by taking into account the physical appearance of the tablets it was decided that the tablets that produced the best results was those which had been produced using 2 tons of pressure. The 1 ton tablets showed promise due to their low disintegration time and acceptable levels of tablet hardness

but as the 1% tablets showed imperfections they would not be suitable for large scale use. Particle size Using the information derived from previous experiments it was established that the ideal concentration of disintegrant required was 5% for the powder mixture and the ideal compressive force needed to produce an ODT was 2 tons. Next came the testing to see the effect particle size has on powder characteristics and tablet properties. The results of the powder characteristic studies can be viewed in table 5. 4 below.

Particle size (um)	Bulk density	Tapped density	Hauser ratio	Carr's index
< 106	0.891	0.391	5.635	7.11
106-250	1.561	0.921	2.318	0.75

Table 5. 4. Results of powder characteristics studies for powders produced containing particles within a certain size range (< 106um and 106-250um) As shown in table 4. 1 the lower the value for both the Hauser ratio and the Carr's index the better the flowability of the powder. It was noted that as the particle size increased the flowability of the powder improved, it had been discussed by Hou and Sun (2008) that the reasoning for the better flowability of the larger particles is due to the weaker bonds between particles. It was stated that smaller particles were able to pack together more closely causing the production of H-bonds and Van Der Waals force stronger than those of large particles, the closer arrangement of particles and possibly more contact points in a powder bed can cause stronger particle-particle interactions therefore the stress required to move the powder bed is higher than a powder bed made up of larger particles. They found that the flowability is affected by the total area of contact between particles (which is greater in smaller particles as they cover a larger surface area) and the closeness between particles. Compressibility increases with average particle diameter. Bigger particles

have less contact surface than smaller ones and then less inter-particle friction is found in the first case as described by Sánchez, Bolarín, Molera et al (2003) resulting in a improvement in flow. It had been noted by Yousef Javadzadeh, Hesam Shariati, and Elmira Movahhed-Danesh (2009) that with fine particle (< 150 um) the forces effecting flow are a combination of frictional force and Van der Waals foces whereas with larger particles (> 150 um) frictional force is the main effecter of powder flow. After the analysis of the data was complete the powder was used for the production of the tablets and then underwent testing to find the effect particle size has on tablet

properties, the results of which can be seen in table 5. 5Particle size (um)Weight (g)Thickness (mm)Diameter (mm)Hardness (N)Friability (%)Disintegration time (s)< 1060. 5 ±0. 012. 5 ±0. 0713. 0 ±0. 0266. 4 ± 9. 822. 2393 ± 6. 28106-2500. 5 ±0. 012. 7 ±0. 0413. 0 ±0. 0251. 5 ± 2. 710. 8723. 8 ± 3. 19

Table 5. 2. Results of tablet testing for tablets produced containing particles within a certain size range (< 106um and 106-250um) with each result being displayed as mean ± SD (except friability)The results were analysed using a t-test to find the find the p value for each results. It was found that the p value for the weight, thickness and diameter were above 0. 05 but the values for disintegration time and hardness were below meaning that there is a significant difference between the groups. The hardness value indicate that the smaller the particle size the greater the tablet strength, a finding supported by Almaya and Aburub (2008) who found that plastic deforming materials, such as MCC, show increasing tablet hardness when in the presence of a lubricant and by Sun & Grant, 2001 and McKenna & McCafferty, 1982 who found the compaction of the smaller

particles results in stronger tablets because of the large surface area available for binding and bonding. It is believed that this occurs due to the close packing of the powder particles causing the production of bonds between the particles which require a large amount of energy to break. This can also be used to explain the reason for the difference in disintegration time, the close packing of the small particles prevents the entry of water molecules into the tablet preventing the swelling of MCC to cause the breakdown of the tablets. It has also been noted that with larger particles porous size increases but the number of pores decrease (Sánchez, Bolarín, Molera et al (2003)), the production of larger pores will result in the entry of more water into the tablet allowing MCC to cause tablet breakdown. The friability of the tablets showed that the smaller particle sizes had a higher degree of mass loss when compared to those made up of larger particles; it is believed that this is related to how the larger particles lock together when undergoing plastic deformation which results in a lower loss on friability testing. So with the final experiment completed it was decided that the 106-250 um particle size range produced the best tablets showing satisfactory results for hardness, friability, disintegration time and high levels of tablet uniformity.