**Particle-particle adhesion energy prediction**

The adhesion energy, $W$, between two contacting particles can be calculated on the basis of their surface energy, $γ\_{i}$, and the real area of contact, $A\_{r}$. For two identical particles of a similar material, with surface energy $γ\_{1}$:

$W=2γ\_{1}A\_{r}$ (1)

The real area of contact is a function of the compressive load, $L$, under which the two particles make contact:

$A\_{r}=\left(\frac{πR^{\*}}{σ^{\*}}\right)\frac{L}{E^{\*}}$ (2)

where, $R^{\*}$ is the effective particle radius, $σ^{\*}$ is the equivalent surface roughness, and $E^{\*}$ is the composite modulus.

For two identical particles of a similar material, these parameters are given by:

$\frac{1}{R^{\*}}=2\frac{1}{R\_{1}}$ (3)

$σ^{\*}=\left(2σ\_{1}^{2}\right)^{0.5}$ (4)

$\frac{1}{E^{\*}}=2\frac{1-ν\_{1}^{2}}{E\_{1}}$ (5)

Hence, the real area of contact, and the adhesion energy, and linearly proportional to the compressive load.

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| Particle no. | Description | R(μm) | σ(nm) | Young's modulus(GPa) | Poisson's ratio(-) | Surface energy (J/m2) | Adhesion energy(aJ) |
| 1 | Cohesive MCC | 26.5 | 1,230 | 25.0 | 0.30 | 0.040 | 28.5 |
| 2 | Non-sieved starch | 6.0 | 168 | 8.0 | 0.30 | 0.040 | 114.5 |
| 3 | Cohesive starch | 3.5 | 109 | 8.0 | 0.30 | 0.040 | 108.5 |
| 4 | Non-sieved pregelatinised starch | 40.0 | 233 | 8.0 | 0.30 | 0.040 | 251.5 |
| 5 | Cohesive pregelatinised starch | 25.0 | 390 | 8.0 | 0.30 | 0.040 | 153.6 |

Assumptions:

(a) 1 μN compressive load between the two contacting particles

(b) surface energy of MCC and starch is 0.040 J/m2

(c) Young's modulus and Poisson's ratio of MCC are 25.0 GPa and 0.30 respectively

(d) Young's modulus and Poisson's ratio of starch are 8.0 GPa and 0.30 respectively

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| Material  | Averageroughness Sa(nm)± | RMS roughness Sq (nm) | P2V roughness Sy (nm) | Adhesion energy(aJ) |
| Cohesive MCC | 875±60 | 1230±115 | 9604±105 | 28.5 |
| Non-sieved starch | 126±38 | 168±60 | 1700±103 | 114.5 |
| Cohesive starch | 81±34 | 109±46 | 703±156 | 108.5 |
| Non-sieved pregelatinised starch | 174±53 | 233±80 | 2934±160 | 251.5 |
| Cohesive pregelatinised starch | 264±109 | 390±212 | 5216±173 | 153.6 |



Figure 1: a) Cohesive MCC, b) Non-sieved starch, c) Cohesive starch, d) Non-sieved pregelatinised starch and e) Cohesive pregelatinised starch

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| Formulations | Angle of repose ($θ$) | Flow property |
| Non-sieved pregelatinised starch | 34.9±2.2 | Good |
| Non-cohesive pregelatinised starch | 30.14±2.3 | Excellent |
| Cohesive pregelatinised starch | 48.44±4.2 | Poor |
| Non-sieved starch | 42.46±2.5 | Passable |
| Non-cohesive starch | 36.16±1.7 | Fair |
| Cohesive starch | 49.3±0.59 |  Poor ( must agitate, vibrate) |
| Non-sieved MCC | 28±1.44 | Excellent |
| Non-cohesive MCC | 25±0.86 | Excellent |
| Cohesive MCC | 39.46±1.29 | Fair |

## 1 and 0.5 % content uniformity of non-sieved carrier using device

Figure : investigation 1% of drug content uniformity using device at 300rpm, no air

Figure : investigation 0.5% of drug content uniformity using device at 300rpm, no air