A Model for the Characterization of Agglomerated Nanoparticle Suspensions

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Introduction

The formulation of poorly water-soluble drugs in many cases utilizes size reduction to micro- or nanometer scale as a mean to increase dissolution rate and enhance bioavailability. With this process the tendency for agglomeration increases and can negate the intended effect.
An agglomeration model for the characterization of nanoparticle suspensions is proposed.

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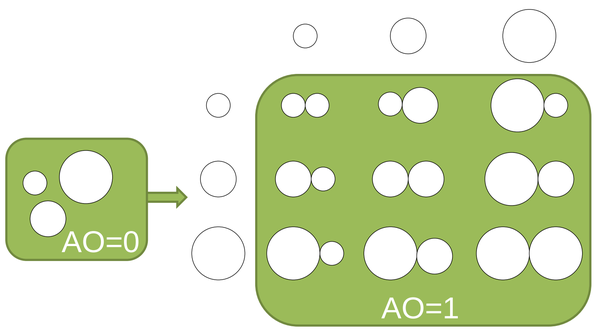
Results & Discussion

Basic Model

If particles are sized below 1 µm particle-particle interactions form agglomerates. They are made up of multiple primary particles. The number of connection points is introduced as agglomeration order (AO). Therefore AO=0 describes the primary particles, AO=1 represents and agglomerate of two individual primary particles as shown below.



It is assumed that statistically every possible size-combination exists in these agglomeration chains and there are infinite primary particles present to form agglomerates of a given order.
Since primary particles, gained for example from (wet) milling, are often following a lognormal distribution, the respective probability density function (pdf) is taken as starting point:

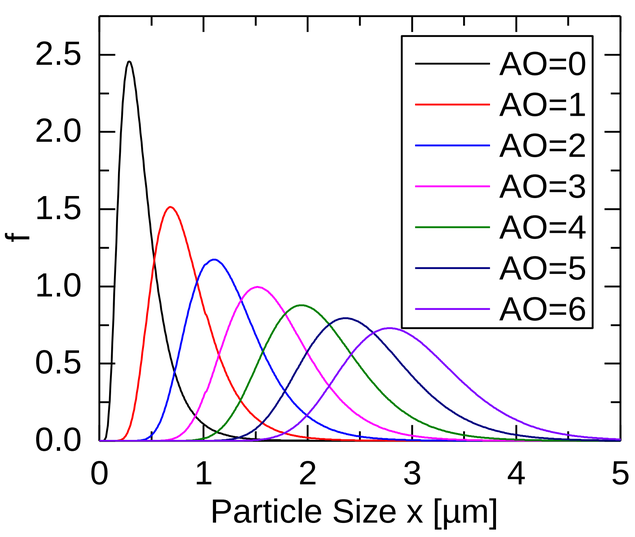
$$f(x \mid \mu, \sigma^2) = \frac{1}{x\sqrt{2\pi\sigma^2}} \exp\left(-\frac{(\ln(x)-\mu)^2}{2\sigma^2}\right)$$

x – particle size
μ, σ – distribution parameters

The agglomeration process is mathematically described by the convolution of two particle size distributions/their respective pdfs.

$$f_{AO+1} = (f_{AO} * f_{AO=0})(x)$$

The numeric convolution of AO 0 to 6 is shown in figure on the right. With increasing agglomeration order the distribution broadens as expected for the agglomeration process .



Advanced Model

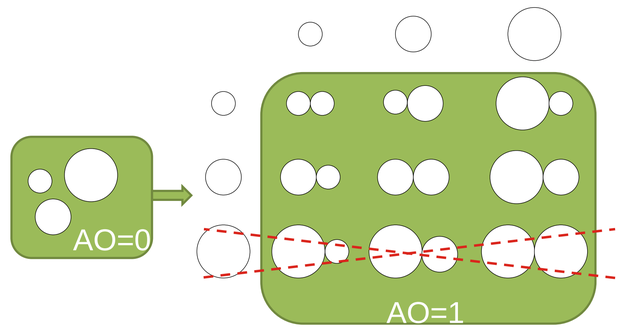
The main drawback of the basic model is that agglomeration of all particles regardless of their size is assumed. In reality smaller particles have a higher tendency to agglomerate. Thus an agglomeration function is applied to each agglomeration order distribution splitting it into a coarse and a fine fraction.

$$F_{ag}\left(x \mid \mu_{ag}, {\sigma_{ag}}^2\right) = \frac{1}{2} - \frac{1}{2}\operatorname{erf}\left(\frac{\ln(x)-\mu_{ag}}{\sqrt{2\sigma_{ag}^2}}\right)$$

$$f_{coarse,AO} = f_{AO} \cdot (1 - F_{ag}) \text{ and } f_{fine,AO} = f_{AO} \cdot F_{ag}$$

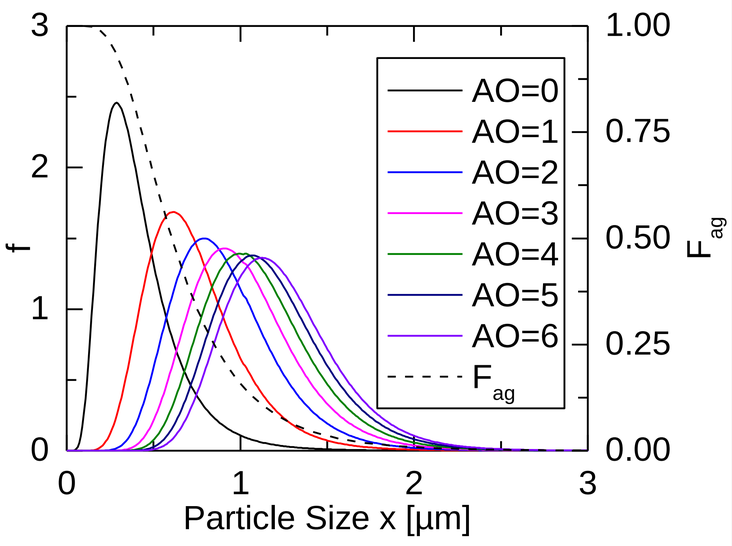
Only the fine fraction is then used for agglomeration with primary particles.

$$f_{AO+1} = (f_{fine,AO} * f_{AO=0})(x) + f_{coarse,AO}$$



The threshold-values μ_{ag} and σ_{ag} indicate the particle size for which agglomeration most likely still occurs. The parameters can possibly be generated from fitting the cumulative oversize function versus grinding time to the first order solution of the population balance model.

The figure on the right shows the influence of the introduced agglomeration function. Since only a small fraction is used for the agglomeration process, the distribution broadens less and changes between different agglomeration order distributions become smaller.



Conclusion

A mathematical model for characterizing the approximate state of agglomerates in nanoparticles suspensions was developed.
It assumes agglomeration as a chain of primary particles, where the number of connection points is described by the agglomeration order (AO)
In contrast to existing models, where only the extent of agglomeration (e.g. 50% of the particles are agglomerates) is shown, this model gives further insight into characteristic behavior of the nanosuspension.

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References

Ely, D.; Garcia, R.; Thommes, M.; Ostwald-Freundlich Diffusion-Limited Dissolution Kinetics of Nanoparticles. Powder Technol., 89, 120-123 (2014).