Project 3:***Crystal Agglomeration: Quantification of Facet Interactions and Analysis of the Solution Spaces between Near Touching Crystal Face***

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Title: The agglomeration of piracetam FIII in different supersaturated solvent systems

Abstract

A number of factors can influence agglomeration in organic solvents. The purpose of this project is to study the agglomeration of piracetam FIII in controlled conditions as a function of solvent choice. The experimental method involves agitating seed crystals of piracetam FIII in different organic solvents at constant supersaturation, temperature, time, and agitation rate, followed by evaluation of the degree of agglomeration. 2 techniques -contact angle measurements and Washburn method were used to evaluate the adhesion free energy of the piracetam FIII seed crystals, and a linear relationship was found between agglomeration and adhesion free energy.

Experiment Method

1. A 100ml supersaturated solution of piracetam (Cs/C = 1.4) was prepared in acetone, ethanol, methanol, 1,4- dioxane or 2-proponol
2. 0.1 g narrowly sieved seeds (100-125 um) were added to the supersaturated solution to grow and agglomerate for 4 min (20 ^{o}C 300 RPM)
3. Agglomerates from the seeded crystallization experiments were collected. 300 particles from each supersaturated solution were examined under an optical microscope to determine the degree of agglomeration (number of crystals in each agglomerate).

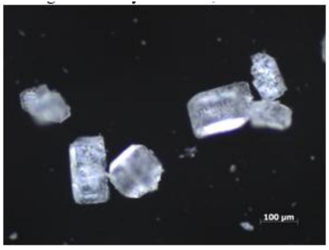


Fig.1 sieved seed crystal l(90-125 μ m)

Adhesion free energy: Contact angle measurement and Washburn method

Adhesion forces are characterized as the thermodynamic free energy of adhesion between solid surfaces in a solution, and can be calculated from the relevant solid-liquid interfacial energies. Unfortunately, solid-liquid interfacial energies cannot be easily measured. In the present work, we determined the contact angle between a solvent and the surface of piractem FIII using traditional contact angle measurements and the Washburn method. The surface free energy was subsequently calculated using Lifsnitz-van der Waals acid-base theory, based on which the adhesion free energy of different faces could be calculated.

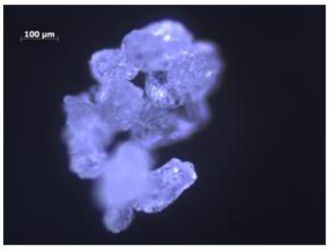
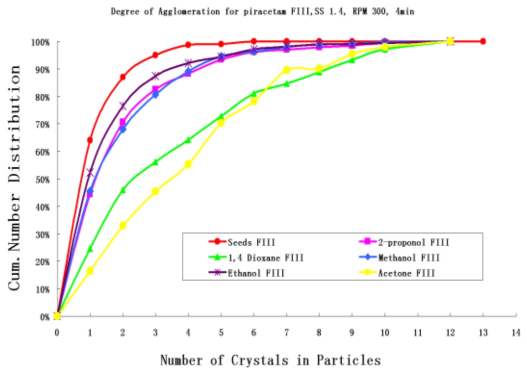
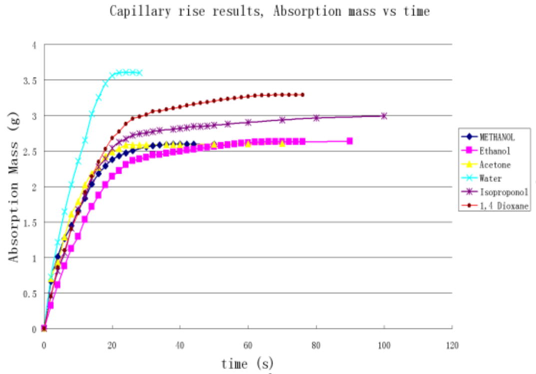


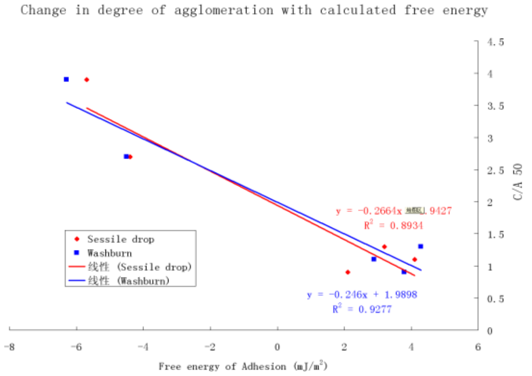
Fig.2 Agglomerates after crystallization

Traditional contact angle measurements allow the contact angle to be determined directly by measurements of the shape of a drop of liquid laid on the smooth solid surface. The contact angle is then determined by the Young equation of the force balance at the three-phase interface: solid, liquid and vapour. The Washburn method is a alternative way for measuring contact angle by using the theory that a liquid penetrates a powder bed in a tube by capillarity forces. There is a linear relationship between the square of the absorption mass of solvent and the time. The slope of the absorption mass of solvent over the time is only determined by the properties of the tube and the wettability of the powder bed, which is expressed as the contact angle.

	Contact Angle Degree				
	Water	Methanol	Ethanol	proponol	Acetone
Sessile droplet	23	≤3	≤3	≤3	≤3
Washburn	35.3	0	4.2	3.9	9.7
	1,4-Dioxane	MeK	Ethyl acetate	Toluene	Hexane
Sessile droplet	11	≤3	≤3	10	9
Washburn	15.5				14.8







Conclusion and Discussion

The degree of agglomeration of Piracetam FIII in Acetone and 1,4 dioxane is much higher than that in the alcohol solvents.

Calculated adhesion free energy may explain different agglomeration behaviour in different solvent system

Future Work:
Study the factor of crystal face in the agglomeration behavior of piracetam FIII

References :

Cashell, C., Corcoran, D., Hodnett, B.K, *The Effect of Amino Acid Additives on the Crystallisation of L-Glutamic Acid.* Crystal Growth and Design, 2005. **5**(2): p. 593-597.