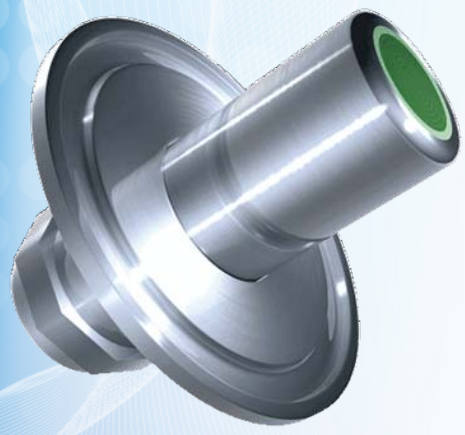
Sponsored by: C-THERM TECHNOLOGIES Ltd.

Thermal Effusivity as a Useful Tool in Powder Charaterization

Guest Speaker: Dr. Rutesh Dave

Long Island University

LIU Pharmacy



AGENDA

- About C-Therm Technologies
- Effusivity - “How it works”
- Thermal Effusivity as a Useful Tool in Powder Charaterization
- Q&A

C-THERM TECHNOLOGIES Ltd.

C-THERM TECHNOLOGIES Ltd.

Non-destructive thermal sensor technology solutions for R&D, production, and QC applications, delivering fast, accurate measurement of **thermal conductivity** and **effusivity** in seconds with virtually unlimited sample size.

Manning Innovation Awards
Prix d'innovation Manning

R&D 100
WINNER

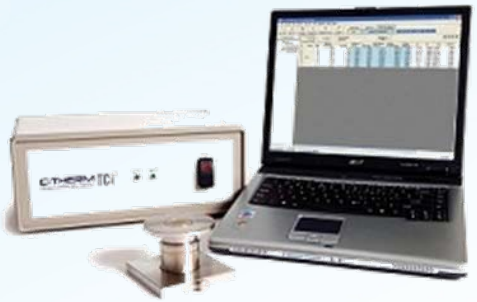
C-THERM PRODUCT LINES

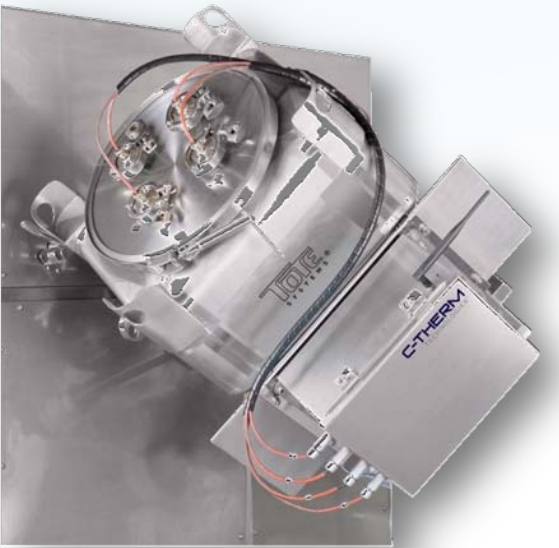
THERMAL CHARACTERIZATION

C-Therm TCi™ Thermal Conductivity Analyzer

Clients include:

- NRC
- Whirlpool
- Kodak
- Philip Morris
- US Navy
- ICI





PHARMACEUTICAL APPLICATIONS

C-Therm ESP™ Effusivity Sensor System

Clients include:

- Patheon
- Wyeth
- BMS
- Astra Zeneca
- Biovail
- USP

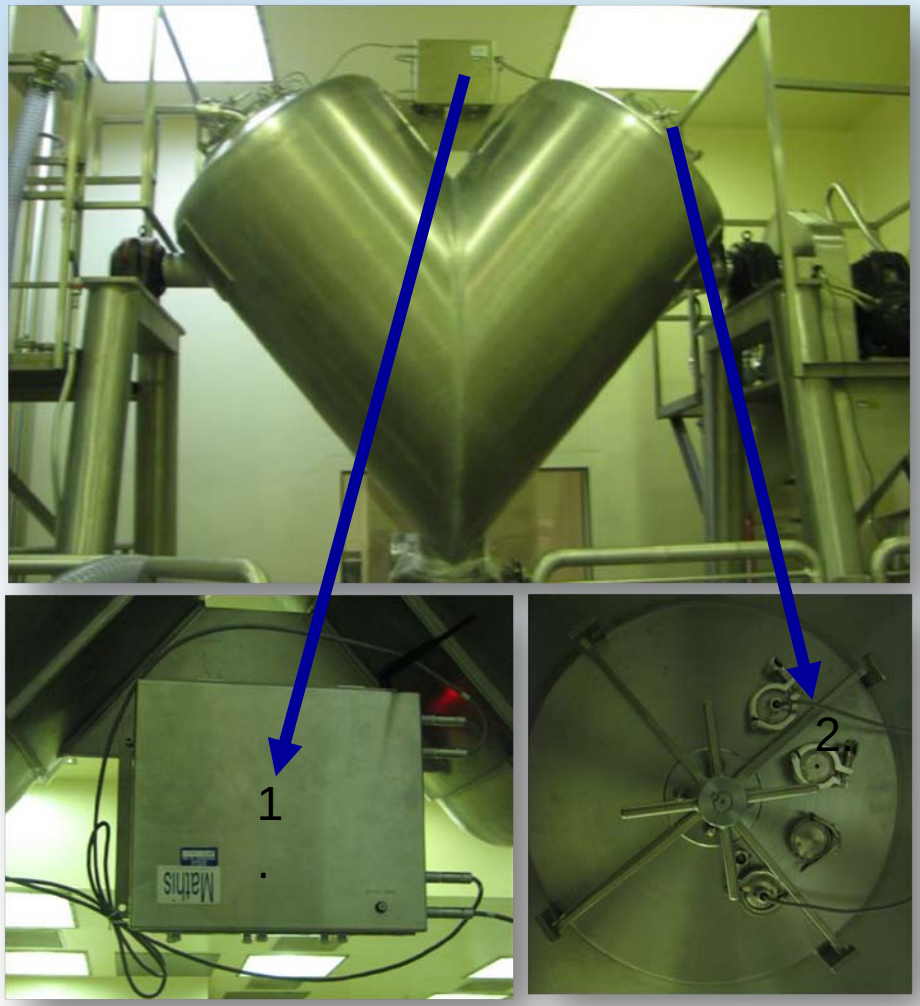
C-THERM TECHNOLOGIES

ESP™ System

Includes: Wireless Controller, 4 Sensors (+spare), Panasonic Toughbook, C-Therm Software, Off-Line Powder Test Kit, Reference Material (PDMS), Operator & Administrator Manual

C-THERM TECHNOLOGIES Ltd.

ESP™ System (Installed)



1 - Mountable controller
- wireless transceiver
- battery with recharger

2 – Retrofitted sensors (2-4) in the lid
- solid state and liquid proof
- 17 mm diameter
- In direct contact with powder

3 - “Toughbook” or HMI options
- dust and spill proof
- integrated wireless
- able to monitor outside suite

4 - Software
- coordinated testing
- feedback for close loop
- multi-unit capability

C-THERM TECHNOLOGIES Ltd.

WHAT DOES IT MEASURE

$$\text{Effusivity} = \sqrt{k\rho c_p}$$

Where :

k = Thermal Conductivity (W/m • K)

ρ = Density (kg/m^3)

c_p = Heat Capacity (J/kg • K)

C-THERM TECHNOLOGIES Ltd.

HOW IT WORKS

Wood feels warm

Metal feels cold

Heat always flows from a hot object to a cold object.

Wood is not a good conductor of heat, so it is **slow** to absorb the heat.

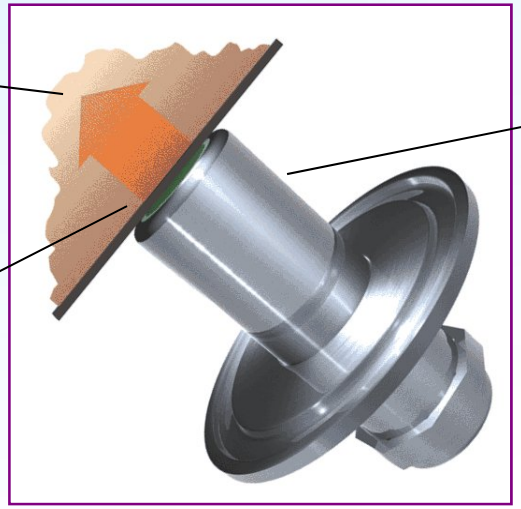
Metal has higher **"thermal effusivity"** so the heat from your hand flows into the metal **quickly** - creating the sensation of it being cold.

C-Therm sensors work like your hand, by **rapidly** determining the **rate** of heat flow from one material to another. Like your hands, our sensors **supply** the heat source *and* **detect** the heat flow. They also have no **sample size** issues, and do not destroy the sample being tested.

C-THERM TECHNOLOGIES Ltd.

HOW IT WORKS

Materials inside the blender have different thermal properties at the onset of blending



Heat is generated by the sensor. Some Heat penetrates the materials, but some is retained.

The heat provided results in a rise in temperature at the interface between the sensor and the sample – typically less than 2˚C.

This temperature rise at the interface induces a change in the voltage drop of the sensor element.

The rate of increase in the sensor voltage is used to determine the thermo-physical properties of the sample material.

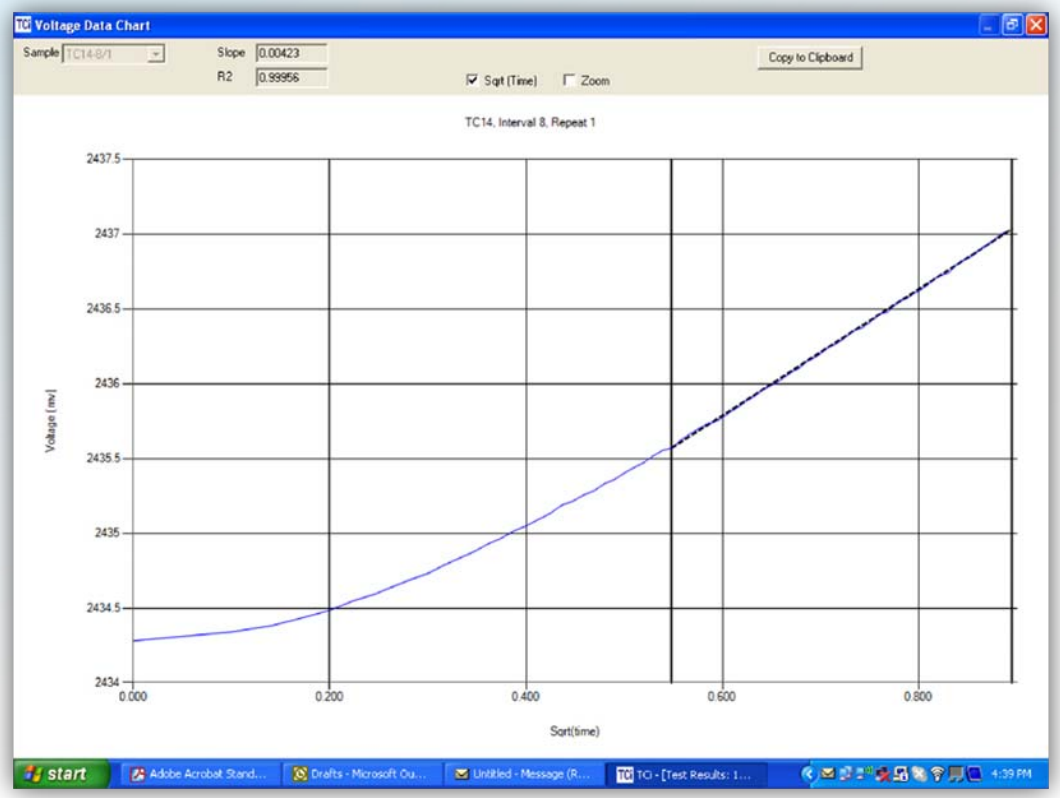
C-THERM TECHNOLOGIES Ltd.

HOW IT WORKS

The thermo-physical properties of the sample material are inversely proportional to the rate of increase in sensor voltage.

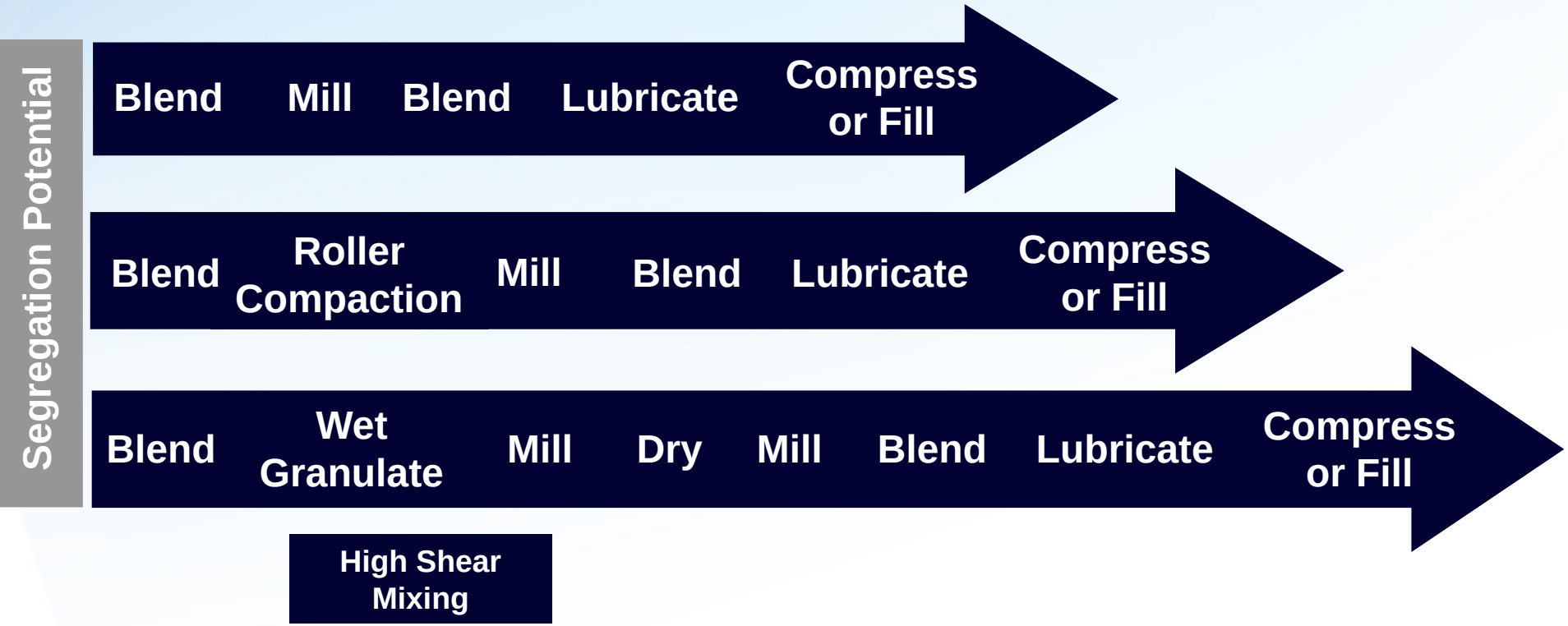
The more thermally insulative the material is – the steeper the voltage rise.

Results are displayed on the system's laptop computer in real time.



C-THERM TECHNOLOGIES Ltd.

SCOPE OF APPLICATIONS FOR EFFUSIVITY



C-THERM TECHNOLOGIES Ltd.

Guest Speaker

Dr. Rutesh Dave

LONG ISLAND UNIVERSITY

C-THERM TECHNOLOGIES Ltd.

Effusivity as a useful tool in powder characterization

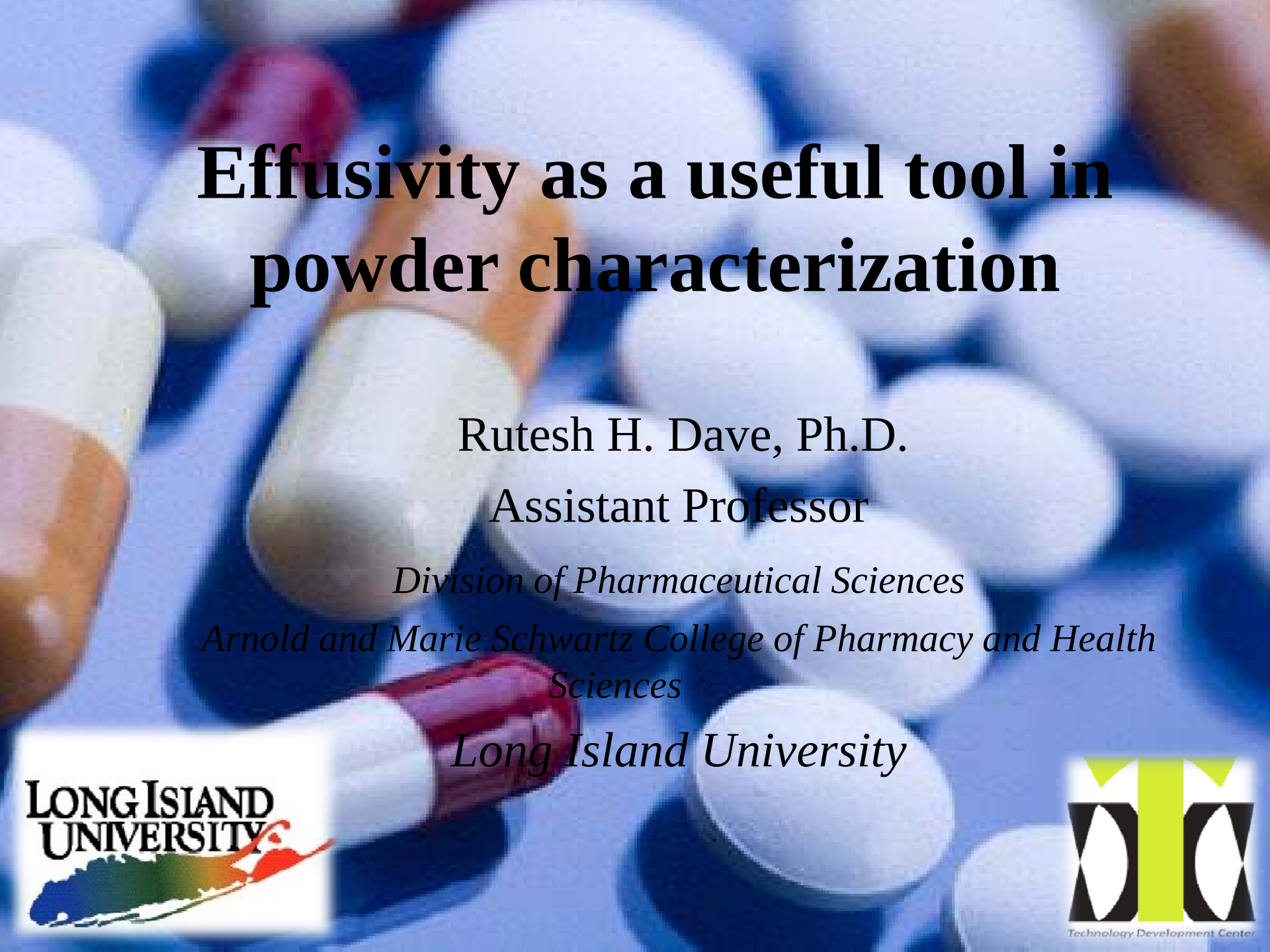
Rutesh H. Dave, Ph.D.

Assistant Professor

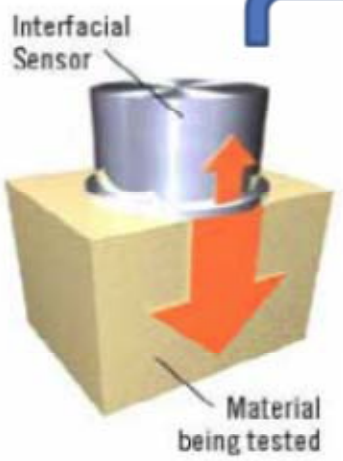
Division of Pharmaceutical Sciences

Arnold and Marie Schwartz College of Pharmacy and Health Sciences

Long Island University



Mechanism of Effusivity



Sensor heat the sample during the testing

Sample absorb some heat

Rest of heat will lead to the temperature increase at the interface

Change in voltage drop of the sensor

Turn to the signal to the ESP computer

Temperature increase proportional to the ability of powder to transfer the heat and other physical properties

Technology Development Center

TCi Probe (Mathis)

LONG ISLAND UNIVERSITY

Technology Development Center

Introduction

- Thermal effusivity is widely used in pharmaceutical industry to detect the difference between solid, liquid, pastes, powder.

- Measuring numerous manufacture process: Blend Uniformity, Roller-compaction processes, fluid bed dry processes, Monitoring End-point of Wet granulation

- Numerous characteristics of samples can be detected by this simple and non-destructive testing, like changes of composition of the powder, particle size, porosity, moisture content, nature surround the particles (air, water).

LONG ISLAND UNIVERSITY

Technology Development Center

End point determination

- Utilizing the conductivity can qualify the quantify the uniformity of the liquid distribution and the uniformity of the wet mass mixing

- Effusivity can also reflect the granule growth and particle size distribution by combine the density. $\text{Effusivity} = \sqrt{\kappa \rho C}$

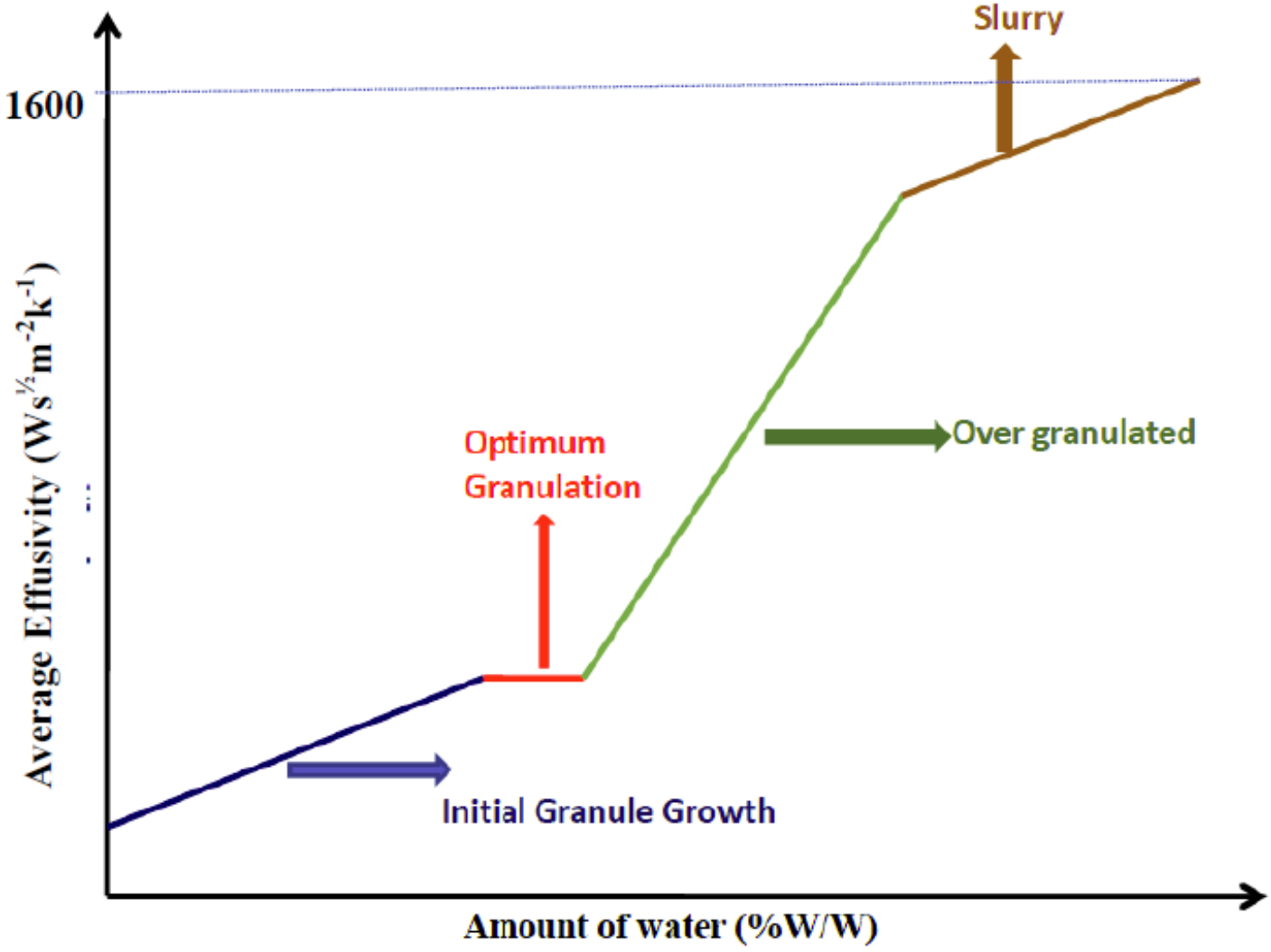
- Water possess the highest Effusivity (1600 $Ws^{½}m^{-2}k^{-1}$) and this makes measuring effusivity an effective tool to monitor the End-point of wet granulation.

- As the amount of water increases effusivity increases. Once water in powder is saturated and the suspension/droplet forms, water appear at the surface of the powder bed and form the slurry which will lead the fact that values to being close to water.

LONG ISLAND UNIVERSITY

Technology Development Center

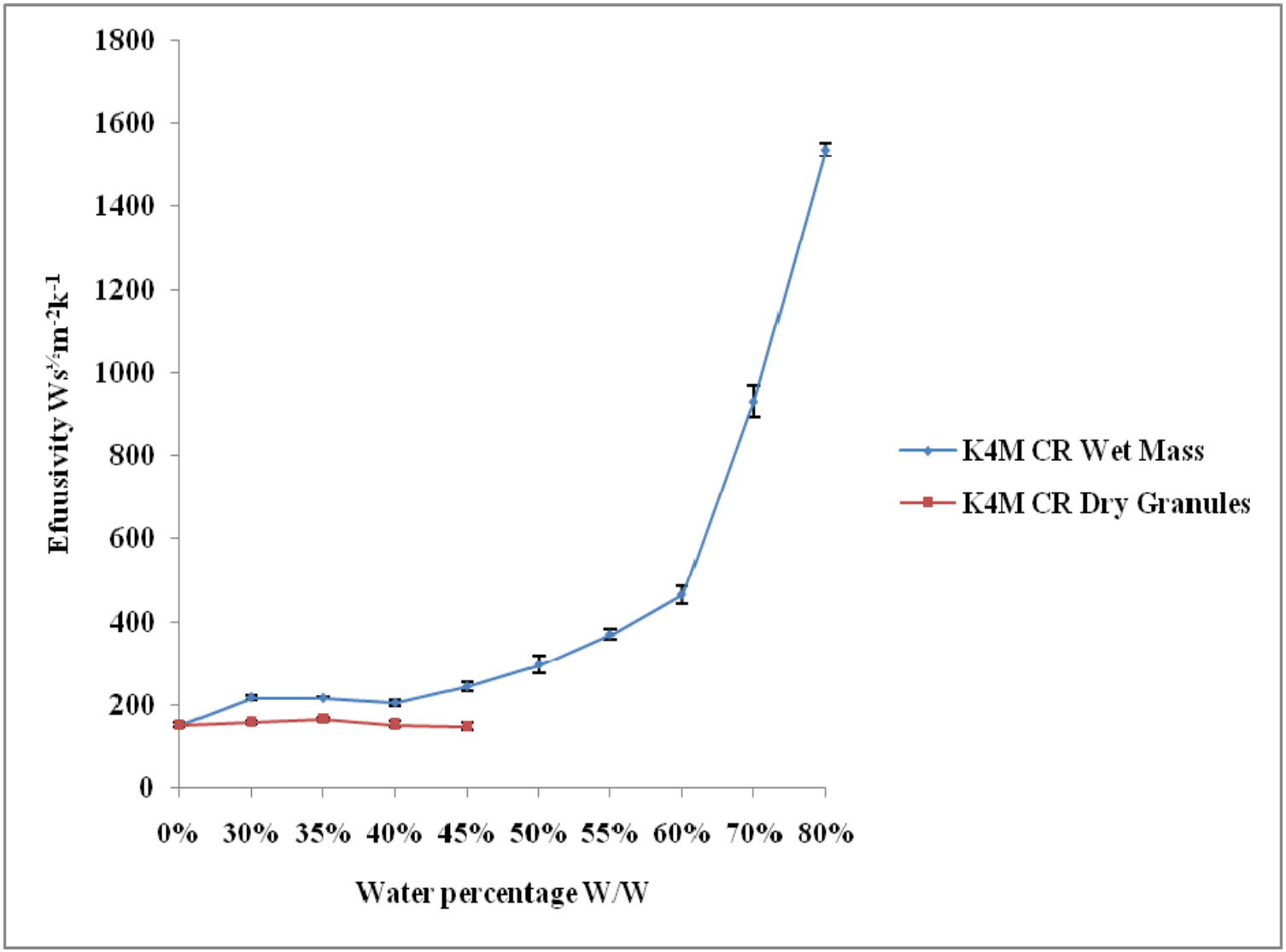
Graphical illustration of end point determination by thermal effusivity



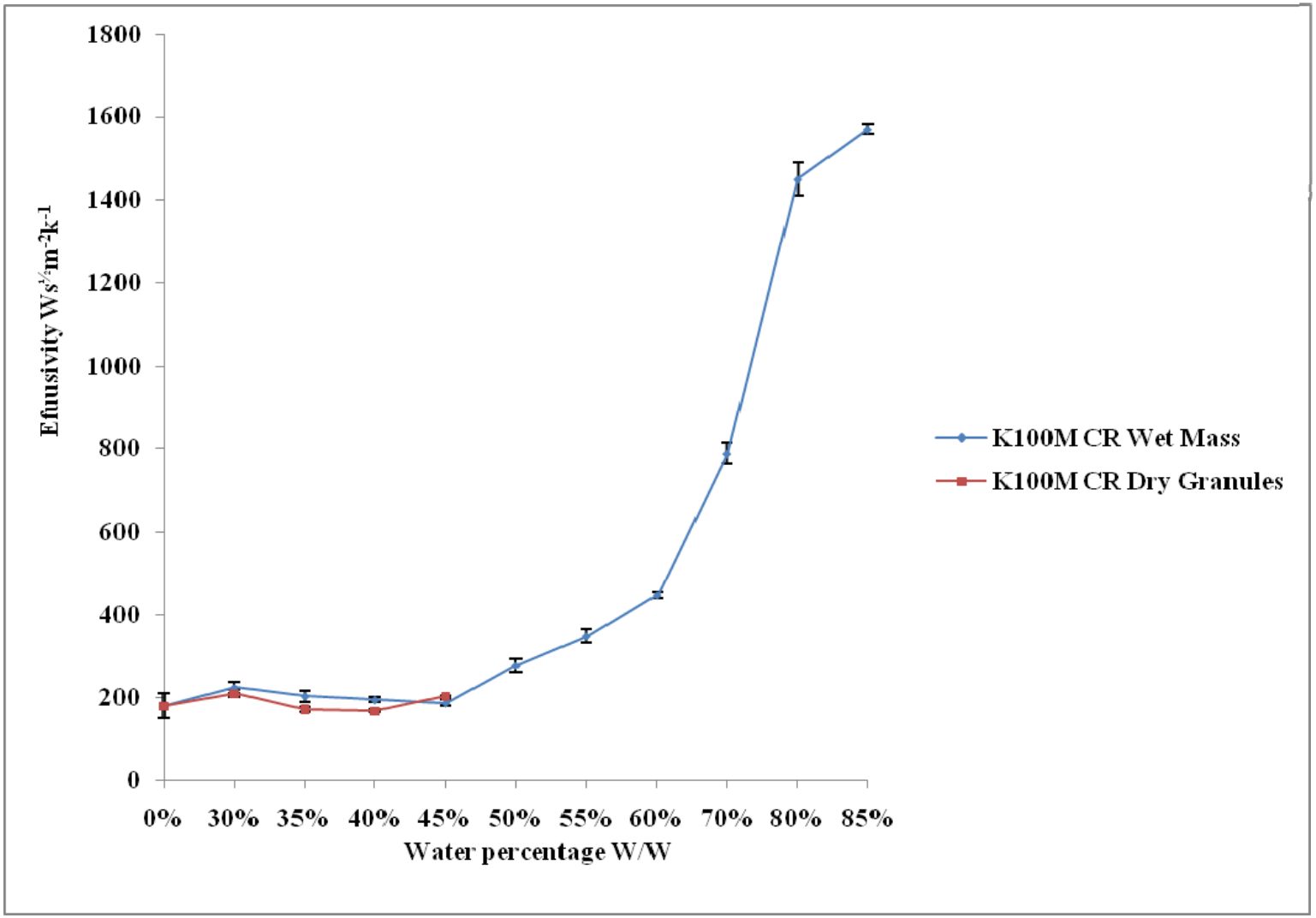
LONG ISLAND UNIVERSITY

Technology Development Center

Effusivity Measurement for K4M CR Lab-scale Wet Granulation



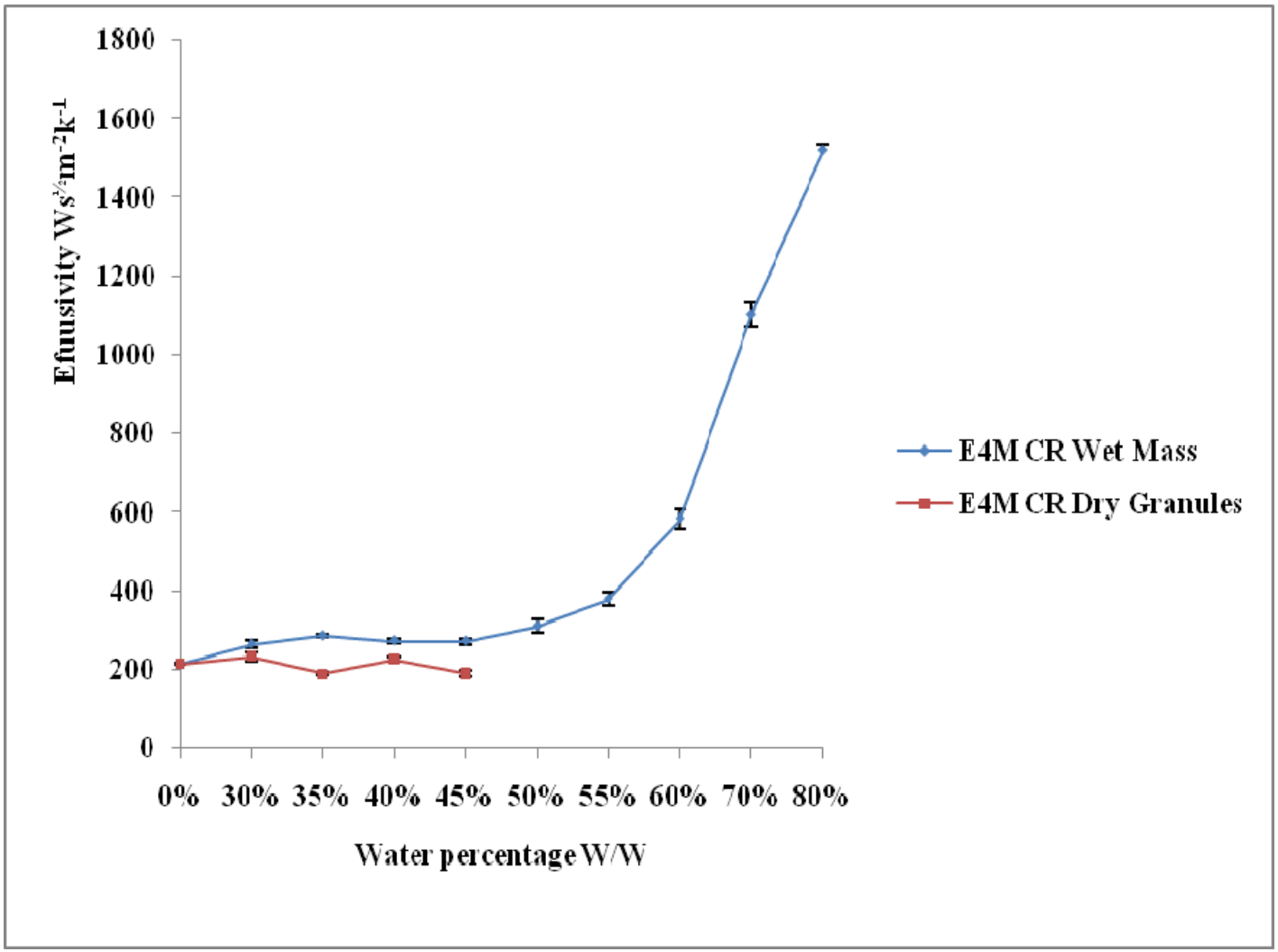
Effusivity Measurement for K100M CR Lab-scale Wet Granulation



LONG ISLAND UNIVERSITY

Technology Development Center

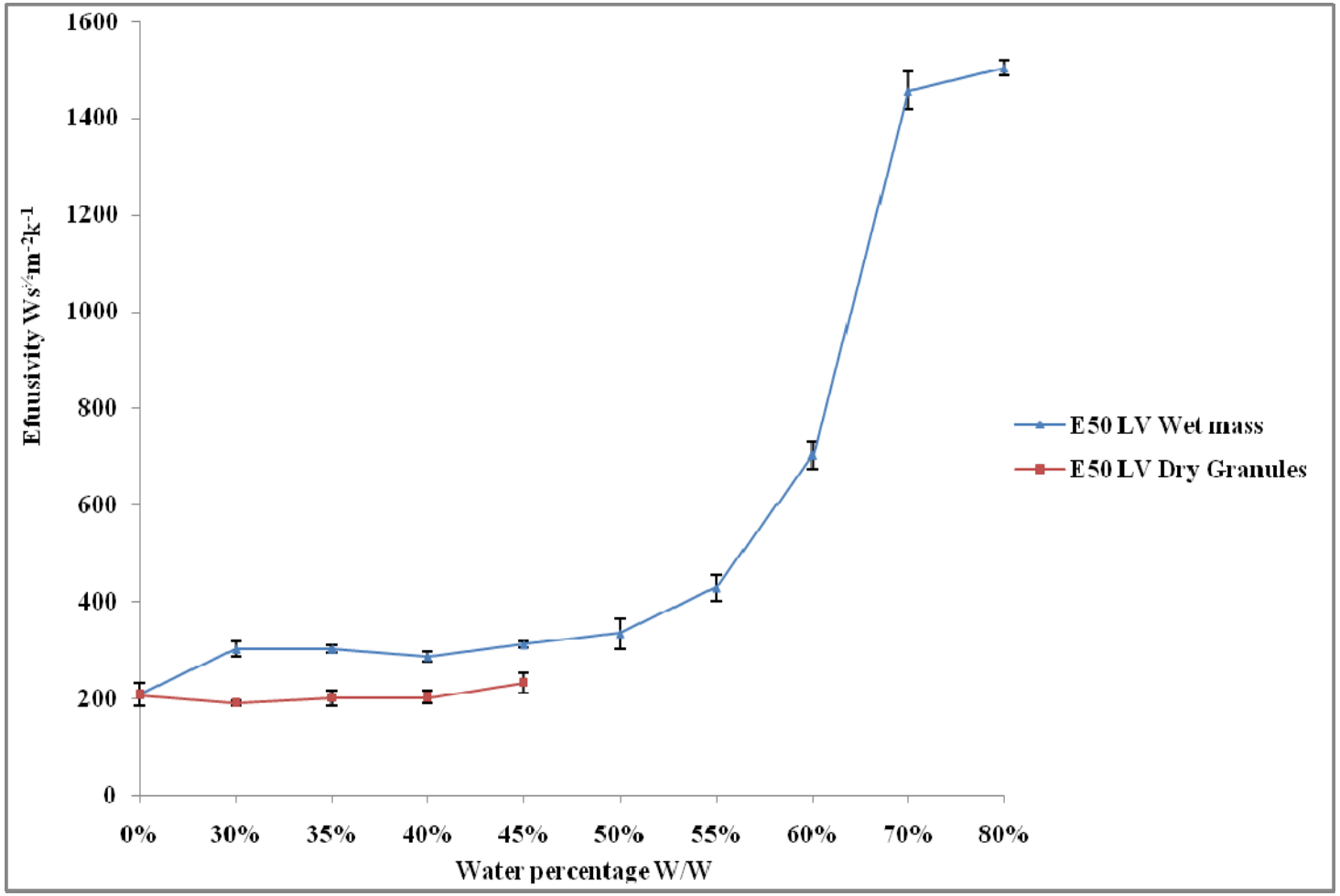
Effusivity Measurement for E4M CR Lab-scale Wet Granulation



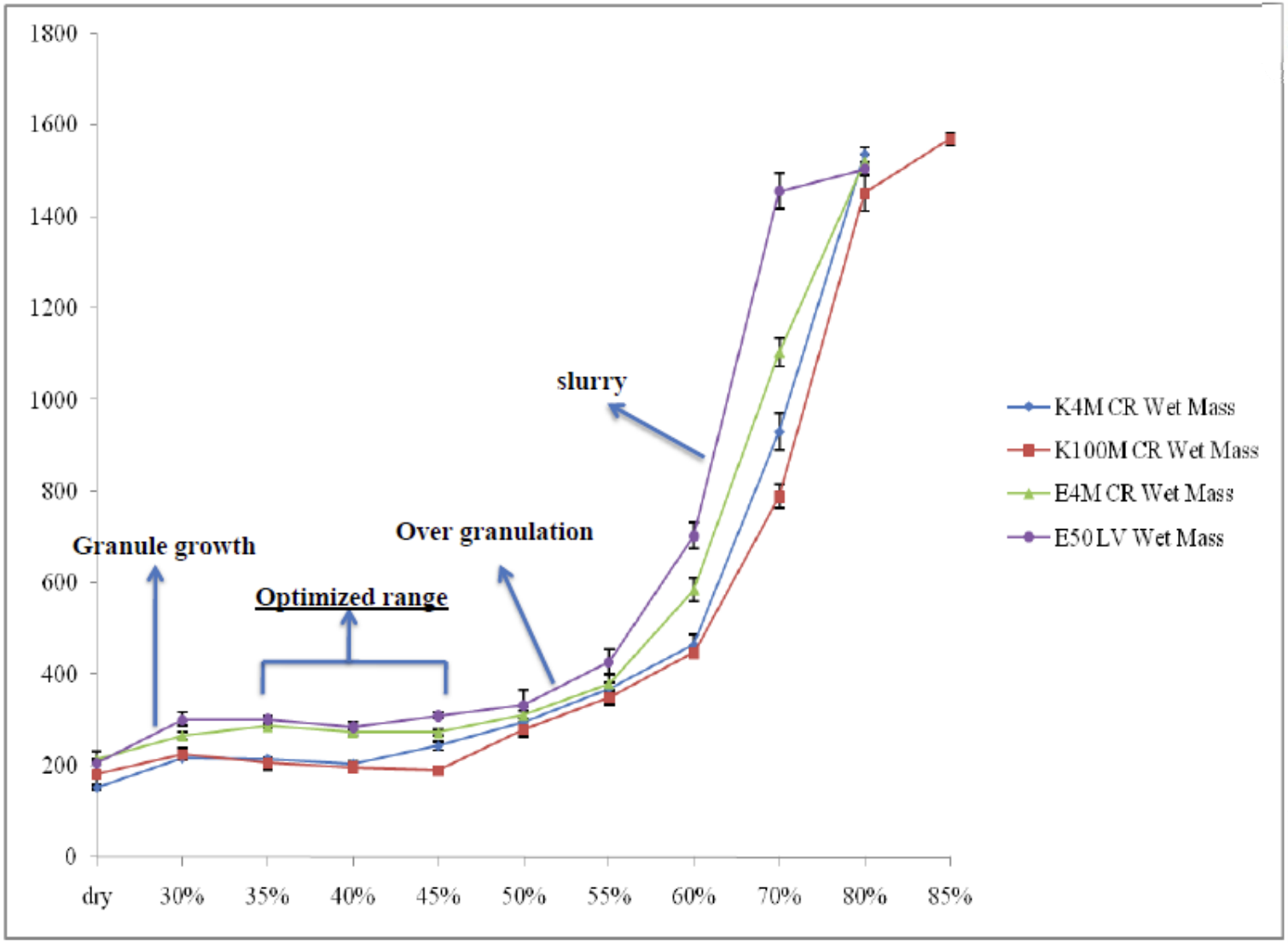
LONG ISLAND UNIVERSITY

Technology Development Center

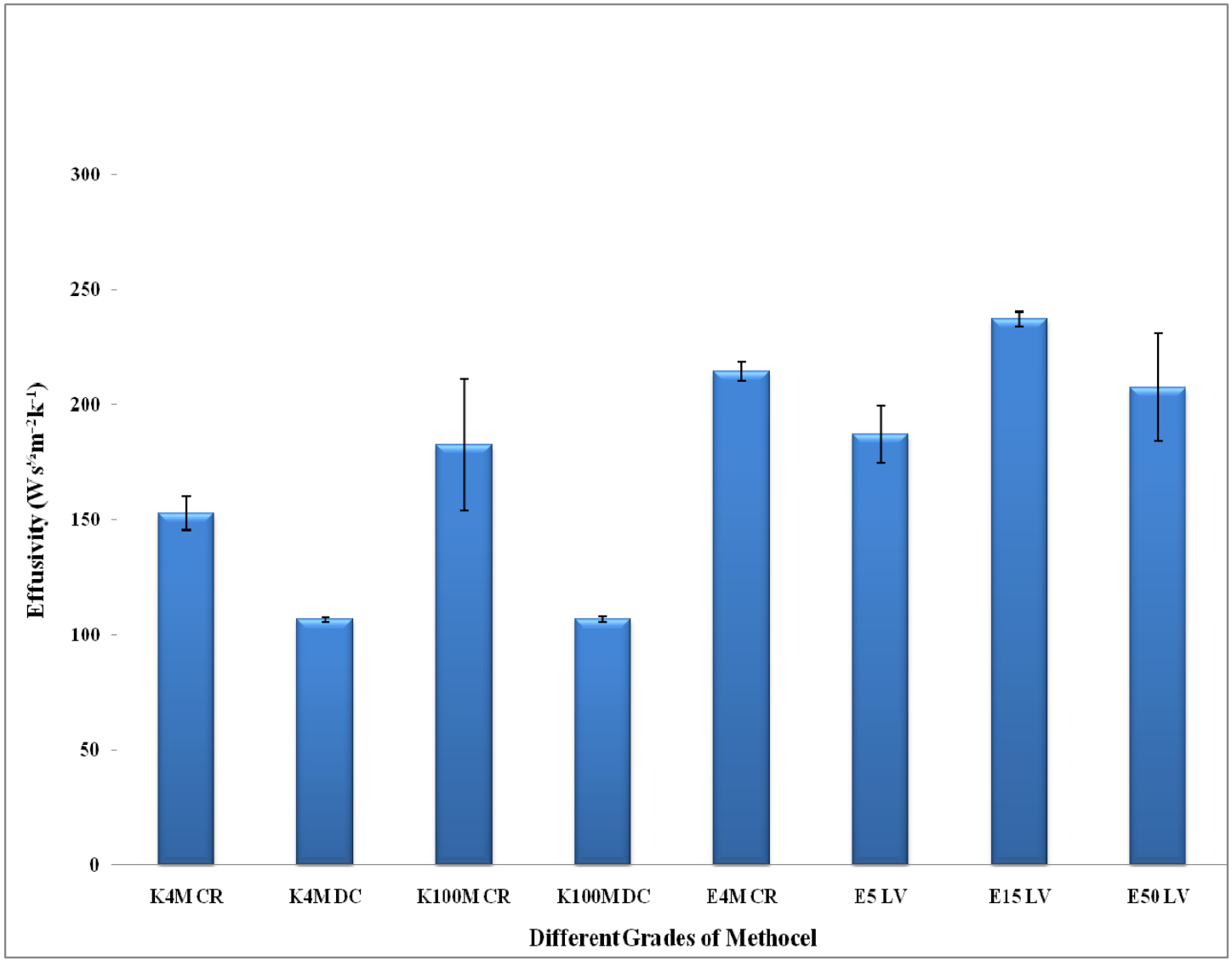
Effusivity Measurement for E50 LV Lab-scale Wet Granulation



Effusivity graph for Different grade HPMC Wet Mass



Thermal Effusivity for Different Grades of HPMC



Effusivity for Dry powder

- Thermal Effusivity data would provide a better understanding for powder density or porosity
- It is directly proportional to the way powder dense itself onto the powder bed
- We can easily see that effusivity for DC <K<E
- Effusivity is low, when compaction occurs, transfer of heat from particle to particle or particle to the outside environment is difficult. Heat will remain in the compact, and will cause the fusion welding among those rough surface particles. This can partly explain why DC and K series have better compressibility over E series.

LONG ISLAND UNIVERSITY

Technology Development Center

Compatibility studies

- Most API's (Active Pharmaceutical Ingredients) do not have material characteristics to be formulated into a dosage form without the aid of excipients

- Selection of excipients based on the characteristics of API, dosage form requirements (modified release or immediate release) and its intrinsic properties (flowability or compressibility of excipients)

- New methodology to differentiate between flow properties of APIs (Active Pharmaceutical Ingredients) and Excipients

- Various excipients having different hydration states show difference in flowability of powders due to water of crystallization in their structure

  - Critical selection can be made from such excipients using different procedures and techniques

LONG ISLAND UNIVERSITY

Technology Development Center

Compatibility studies

- Materials: DCP- A, DCP-D and Acetaminophen were used to determine compatibility studies.

DCP-A	DCP-D
263.43 (± 1.36)	349 (± 2.06)

DCP (Dibasic Calcium Phosphate) anhydrous and dihydrate

- Water having highest effusivity leads to materials giving high effusivity values with water molecules in the powder

LONG ISLAND UNIVERSITY

Technology Development Center

Compatibility studies

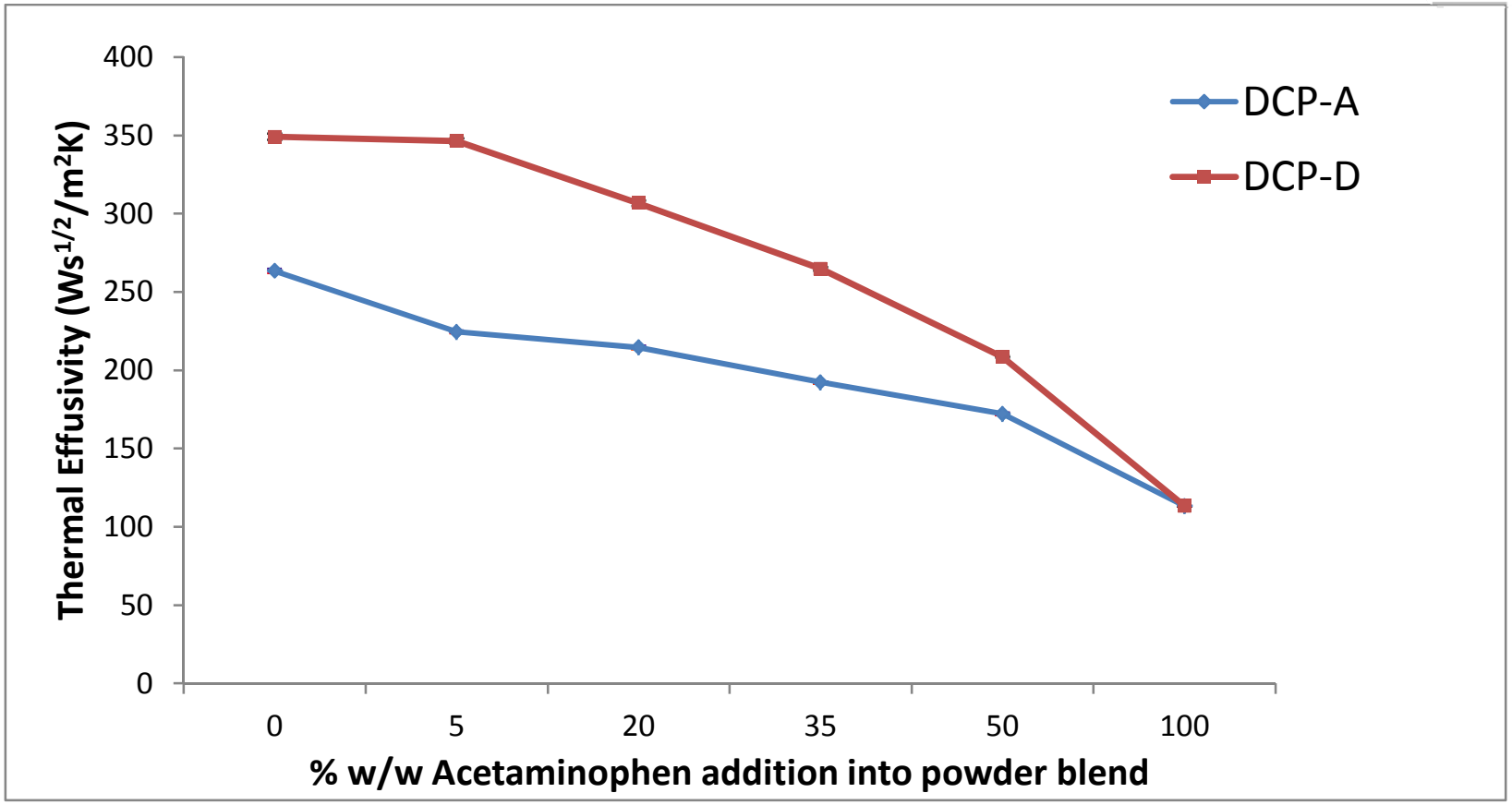
- APIs have ability to change the properties of excipients
- Excipients should resist the change in the properties
- Acetaminophen (APAP) being cohesive powder have very low effusivity values

Acetaminophen (APAP)	**113.3 (± 0.21)**

LONG ISLAND UNIVERSITY

Technology Development Center

Compatibility Studies



- Effusivity of air is less leads a powder blend with more air-pockets having relatively less effusivity. Acetaminophen leading to more air pockets in the blend decreases the effusivity of total blend

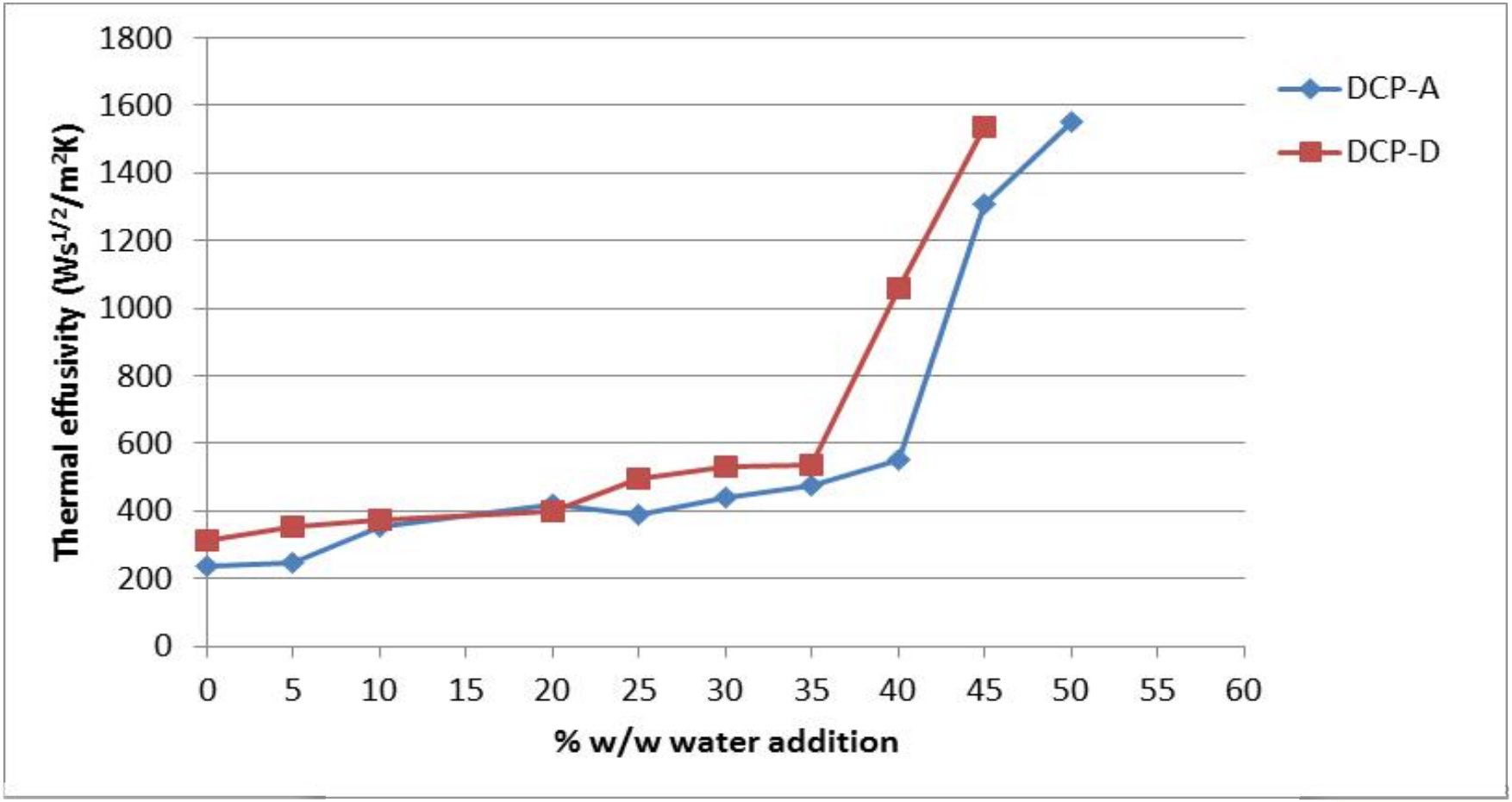
Compatibility studies

- To determine the effect of different hydrate states on wet granulation end point
- DCP-A and DCP-D were used with water as a wet granulating agent
- Change in end point with use of different hydrate states of excipient the following graph explains the change by 5%w/w water addition

LONG ISLAND UNIVERSITY

Technology Development Center

Change in wet granulation end point



LONG ISLAND UNIVERSITY

Technology Development Center

Conclusion

- Thermal Effusivity can be utilized to determine the end-point of wet granulation
- Analyze difference between various hydrates
- Be able to detect small change in water addition
- Perform compatibility studies

LONG ISLAND UNIVERSITY

Technology Development Center

Acknowledgements

- Haichen Nie
- Maitri Trivedi

QUESTIONS?

Adam Harris
Managing Director
C-Therm Technologies Ltd.

Email: aharris@ctherm.com

Tel: (506) 461-7203

www.ctherm.com

C-THERM TECHNOLOGIES Ltd.