CAPSTONE SUMMER PROJECT 2019

Thermal Hazards in the Pharmaceutical Industry

Industry Sponsor: AMGEN

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INTRODUCTION

The U.S. Chemical Safety Board conducted a study in the year 2002 that identified 167 industrial process safety incidents that involved runaway reactions between the years, 1985 and 2001.[1] In an exothermic process, when the rate at which heat is released exceeds the rate at which heat is being removed, a runaway reaction develops. Commercial reactors behave like adiabatic vessels (negligible heat losses to surroundings due to large surface to volume ratios) and therefore, the temperature inside the reactor rises at a rapid rate and eventually, leads to an explosion if appropriate measures are not taken.

Risk is often defined as a product of consequence and frequency. In the event of a runaway, the time period between the onset of the runaway reaction or self-heating of the reaction mixture and the point at which the rate of heat production is maximum is called the 'Time to Maximum Rate under Adiabatic Conditions' or the TMR_{ad}. The resulting rise in temperature is called the 'Adiabatic Temperature Rise', ΔT_{ad}. While the TMR_{ad} is a measure of likelihood of occurrence of a runaway, the ΔT_{ad} is a measure of consequence of the runaway reaction.[2]

The Stoessel Criticality Index classifies exothermic processes with a TMR_{ad} of 24 hours or greater as low risk scenarios.[2] The TMR_{ad} is a function of the temperature at which the process is being held. From a safety standpoint, the temperature at which the TMR_{ad} is equal to 24 hours is therefore, important and is known as the T_{D24}.

The TMR_{ad} and T_{D24} are characteristics of reactive chemical hazards that can be evaluated by analyzing data obtained from calorimetric experiments. For the purpose of thermal hazard evaluation studies, Differential Scanning Calorimetry is the most commonly used technique. Other commonly used techniques include Accelerating Rate Calorimeter (ARC), Advanced Reactive

System Screening Tool (ARSST), Dewar Calorimeter, Reaction Calorimeter (RC), and Vent Sizing Package 2 (VSP2). The main objective of this project was to analyze data obtained from experiments run on the ARSST using mathematical methods described in literature and extract information about the TMR_{ad} and the T_{D24}.

LITERATURE REVIEW

An extensive literature survey was conducted to obtain information about the various mathematical methods and software packages available to calculate the values of the TMR_{ad} and the T_{D24} for a given system by analyzing calorimetric data.[3] For the purpose of this report, main ideas presented in four relevant papers are discussed.

In 1980, Townsend et.al, discussed in their paper, the use of an Accelerating Rate Calorimeter for thermal hazard evaluation. Concepts of 'Time to Maximum Rate' and 'Thermal Inertia' were introduced and their importance with respect to engineering considerations in order to prevent runaway reactions was briefly discussed. The paper also presented an integral equation that can be used to evaluate the TMR_{ad} based on reaction kinetics.[4]

Keller et.al (1997) proposed a systematic procedure for the assessment of thermal risk based on dynamic and isothermal DSC experiments. The authors also introduced a linear correlation between the onset temperature and the T_{D24} (referred to as the Model Based Estimation Method). In this paper, kinetic parameters were evaluated for zero-order, first-order and autocatalytic models.[5]

Using the concepts developed and discussed by Keller et.al in 1997 and T_{D24} results from 180 adiabatic experiments, Pastre et.al (2000), confirmed that the Model Based Estimation Method gave values that were more conservative than those obtained from adiabatic experiments on the

Dewar Calorimeter. The paper also compares these values with the industrially used 100 K and 50 K rules. They concluded that at higher temperatures, the 100 K and 50 K rules were less conservative and at lower temperatures, they were too restrictive.[6]

Kossoy et.al (2015) compared two different approaches (referred to as the Standard Approach and the Expert Approach) used to evaluate and analyze data obtained from adiabatic experiments. The Standard Approach involves evaluation of kinetics using the Arrhenius Linearization Method, the Enhanced Fisher's Method to Reconstruct the Self-Heat Rate Curve and the Frank-Kamenetskii Method to calculate the TMR_{ad} and the T_{D24}. The Expert Approach on the other hand, uses non-linear optimization and integral methods to calculate the kinetics and simulate adiabatic conditions. Typically, these calculations are performed by a commercially available software package. While the Standard Approach is easy to use, the Expert Approach is more reliable in situations where the reactions are complex (multi-stage) and/or non-autocatalytic. They concluded that for simple (single-stage) non-autocatalytic reactions and initial screening studies, the Standard Approach is a more practical option.[7]

TECHNICAL DESCRIPTION

Calorimetric data obtained from experiments run on the ARRST was analyzed using mathematical methods to obtain the values of the TMR_{ad} and the T_{D24}. These experiments had been conducted by an undergraduate researcher, Matthew Jacob in the fall of 2018. Experiments had been conducted on samples of pure DMSO (Dimethyl Sulfoxide), and binary mixtures of DMSO and four acids, namely, Acetic Acid, Phenol, Methanol and Water. This section of the report provides a brief overview about the mathematical methods used to analyze the experimental data.

Nomenclature

T_{on} = Onset Temperature (Temperature at which onset of self-heating occurs), K

ΔT_{ad} = Adiabatic Temperature Rise = $(T_m - T_{on})$, K

T_m = Temperature at which self-heat rate is maximum, K

$\propto = (T - T_{on})/\Delta T_{ad}$, Reactant Conversion Term

T_f = Final Temperature, K

k_0 = Pre-exponential factor, 1/min

c_p = Specific Heat Capacity, kJ/kg

n = Order of the reaction

R = Universal Gas Constant = 8.314 J/mol K

E = Activation Energy, J/mol

Φ = Thermal Inertia (Phi-Factor)

t = time, min

$Q_\infty = \Phi\, c_p\, \Delta T_{ad}$ = Specific Heat Effect, kJ/kg

Data Analysis

In evaluating the TMR_{ad} and the T_{D24}, one must follow three steps, namely, Evaluation of Reaction Kinetics, Correction of Experimental Data for Thermal Inertia and Estimation of the TMR_{ad} and the T_{D24}.[7]

1) <u>Evaluation of Kinetics</u>[8]

The differential iso-conversional approach is adopted, which assumes that the rate of the reaction in terms of conversion (α) is a function of temperature (T). It is also assumed that the following rate law is obeyed by the reaction.

$$\frac{d\alpha}{dt} = k_o \exp\left[\frac{-E}{RT}\right](1-\propto)^n \qquad (1)$$

To evaluate the kinetic parameters, the activation energy (E) and the pre-exponential factor (k_o), the Arrhenius Linearization technique is applied to the rate law.

$$\ln\frac{d\alpha}{dt} = \ln k_0 + n\ln(1-\propto) - \frac{E}{RT} \qquad (2)$$

For the purpose of this project, reaction orders 0 and 1 were assumed to give conservative results. Higher reaction orders give less conservative results because the rate in those cases is assumed to decrease with a decrease in concentration of the reactant. Multiple linear regression was also applied to the Equation (2) in order to evaluate the order of the reaction in addition to the kinetic parameters, k_o and E.

2) Correction of Experimental Data for Thermal Inertia

The ARSST is a pseudo-adiabatic calorimeter. Therefore, the data must be corrected for purely adiabatic conditions. In order to do this, a parameter called the thermal inertia (ϕ-factor) is used which can be calculated using the following expression.[9]

$$\phi = 1 + \frac{(\text{Mass} \times \text{Specific Heat Capacity})_{Container}}{(\text{Mass} \times \text{Specific Heat Capacity})_{Sample}} \qquad (3)$$

After evaluating the thermal inertia, the following four steps were followed to correct the data for purely adiabatic conditions. This method is known as the Enhanced Fisher's Method.[7]

1. Adiabatic Onset Temperature Evaluation

$$\frac{1}{T_{on,ad}} = \frac{1}{T_{on}} + \frac{R}{E}\ln\phi \qquad (4)$$

2. Adiabatic Temperature Course Evaluation

$$T_{ad}(t) = T_{on,ad} + \phi\,[T(t) - T_{on}] \qquad (5)$$

3. Adiabatic Self-Heat Curve Reconstruction

$$\left(\frac{dT}{dt}\right)_{ad} = \phi\left(\frac{dT}{dt}\right)_{experimental} \exp\left[\frac{E}{R}\left(\frac{1}{T} - \frac{1}{T_{ad}}\right)\right] \qquad (6)$$

4. Adiabatic Time Scale Reconstruction

$$t = \int_{T_{on,ad}}^{T_{ad}} \frac{dT}{(dT/dt)_{ad}} \qquad (7)$$

3) Estimation of the TMR_{ad} and the T_{D24}

Three different approaches were used to estimate the TMR_{ad} and the T_{D24}. They are as follows:

a) The Frank-Kamenetskii Method[7]

This method assumes that the reaction follows zero-order kinetics.

$$TMR_{ad} = \frac{c_p R T_{on}^2}{k_o Q_\infty E} \exp\left(\frac{E}{R T_{on}}\right) \qquad (8)$$

Kinetic parameters evaluated in step one (Evaluation of Kinetics) for the zero-order assumption were used to determine the TMR_{ad} using Equation (9). With the help of Equation (9) and the MS-Excel Solver Add-in, the value of T_{on} for which the TMR_{ad} is 1440 minutes (or 24 hours) was calculated, which is essentially the value of the T_{D24}.

b) Model Based Estimation Method[5]

Keller et.al (1997) formulated a linear correlation between the onset temperature (T_{on}) and the T_{D24}. The equation was found to have a correlation factor of 0.9998.

$$T_{D24}[K] = 0.65 T_{onset}[K] + 50 \qquad (9)$$

c) Integral Equation Derived from Rate Law

An equation for the TMR_{ad} can be derived from the rate law given in Equation (1).

$$TMR_{ad} = \int_{T}^{T_m} \frac{dT}{k \exp\left[\frac{-E}{RT}\right]\left(\frac{T_f - T}{\Delta T_{ad}}\right)^n \Delta T_{ad}} \qquad (10)$$

Equation (10) was evaluated between the limits, T_{on} and T_m, using *Wolfram Mathematica* to calculate the value of the TMR_{ad}. To obtain the value of the T_{D24}, a value of 1440 minutes was assigned to the TMR_{ad} and the 'FindInstance' function was used.

The TMR_{ad} and T_{D24} were evaluated for reaction orders 0, 1 and for the value of reaction order obtained by applying multiple linear regression to the Arrhenius Linearization Equation (see Equation (2)).

Prediction by Software

The Advanced Kinetics and Technology Solutions Thermal Safety Software can evaluate the T_{D24} based on experimental data obtained from 3-4 isothermal DSC runs at specified heating rates. The software uses Model Free Kinetics and Simulation to make predictions about the TMR_{ad} and the T_{D24}.[3] The value of the T_{D24} predicted by the software was compared with the value obtained from data analysis using the mathematical methods described previously.

Experimental Validation

To validate the results obtained from analyzing calorimetric data obtained from temperature ramp tests on the ARSST, an isothermal hold experiment was conducted. The experiment involved heating the sample to a temperature equal to the T_{D24} calculated using the mathematical methods described in the previous section and holding it at that temperature for a period of 24 hours. If a runaway reaction was observed, it would experimentally validate the accuracy of the results obtained by data analysis.

RESULTS AND DATA INTERPRETATION

Values of TMR_{ad} and T_{D24} were calculated using methods described in the Technical Description section of the report for the following systems: Pure DMSO (2 experimental data sets were available), DMSO and Acetic Acid (9 to 1 molar ratio), DMSO and Acetic Acid (5 to 1 molar ratio), DMSO and Phenol (9 to 1 molar ratio), DMSO and Phenol (5 to 1 molar ratio), DMSO and Methanol (9 to 1 molar ratio), DMSO and Methanol (5 to 1 molar ratio) and DMSO and Water (9 to 1 molar ratio). For the purpose of this report, the results of the DMSO Phenol (5 to 1 molar ratio) system are discussed in detail. This particular system was chosen to be discussed in detail because Mr. Derek Brown (Scientist at Amgen) was able to run DSC tests on a sample of DMSO and Phenol (5 to 1 molar ratio) and have the AKTS software predict the value of the T_{D24} for the same. We were also able to run an isothermal hold experiment using the ARSST on Purdue campus for the same system at the calculated value of the T_{D24}. The results for the other 8 systems are presented in a consolidated fashion towards the end of this section.

DMSO Phenol System (5 to 1 Molar Ratio)

Temperature Vs Time Data

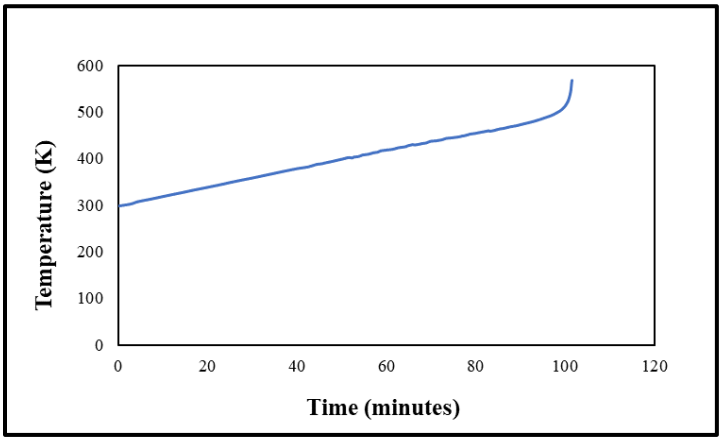

Figure 1: Temperature Vs Time Data for DMSO Phenol (5 to 1 molar ratio)

Determination of the Onset Temperature

From the raw data, the rate of temperature change vs the inverse of temperature data is plotted. Using this graph, the onset temperature is obtained. For this system, the onset temperature was found to be 198.15 ºC.

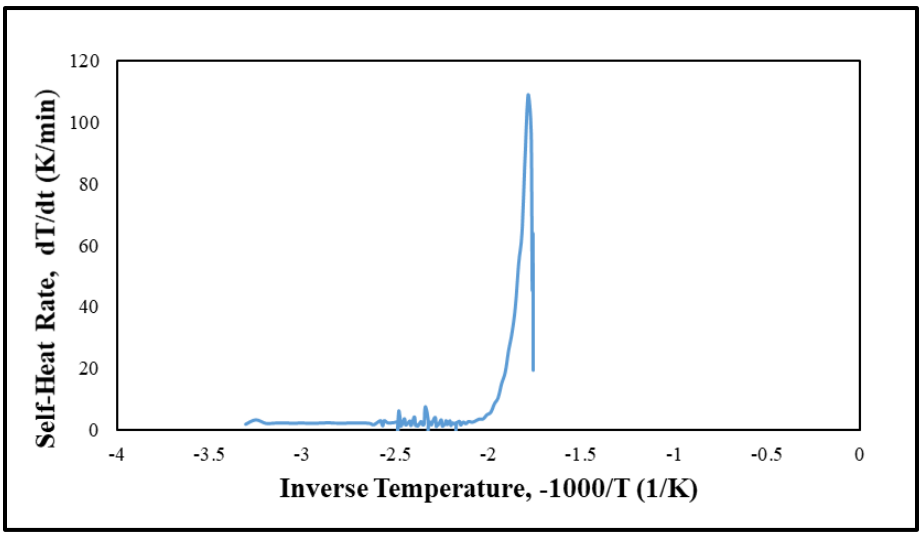

Figure 2: Onset Temperature Determination

Evaluation of Kinetics

It was assumed that at the onset temperature, the decomposition reaction takes off resulting in an exotherm. Using the differential iso-conversional approach, conversion factor (α) is calculated.

$$\alpha = \frac{T - T_{on}}{T_{on} - T_{max}} \qquad (11)$$

a) Zero Order

It was first assumed that the reaction follows zero-order kinetics. Equation (7) then reduces to the following expression.

$$\ln \frac{d\alpha}{dt} = \ln k_0 - \frac{E}{RT} \qquad (12)$$

Reaction rate in terms of conversion (dα/dt) was obtained using the following relation.

$$\frac{d\alpha}{dt} = k_o \exp\left[\frac{-E}{RT}\right] \qquad (13)$$

Logarithm of the rate of reaction was then plotted against the inverse of the temperature. Linear regression was applied to this data to obtain a straight line equation with an R-Squared value of 0.9826.

$$y = -12520x + 22.42 \qquad (14)$$

By comparing equations 12 and 14, a value of 5.45×10^9 min^{-1} was obtained for the pre-exponential factor and a value of 104.09 kJ/mol for the activation energy.

b) First Order

We then assumed that the reaction obeyed first order kinetics. In this case, Equation (7) reduces to the following expression.

$$\ln\left[\frac{d\alpha/dt}{1-\alpha}\right] = \ln k_0 - \frac{E}{RT} \qquad (15)$$

$\ln\left[\frac{d\alpha/dt}{1-\alpha}\right]$ was plotted against the inverse of temperature and after applying linear regression to the data, a straight line equation with an R-Squared value of 0.9540 was obtained.

$$y = -19535\,x + 36.994 \qquad (16)$$

The pre-exponential factor was 1.16×10^{16} min^{-1} and the activation energy was 162.41 kJ/mol.

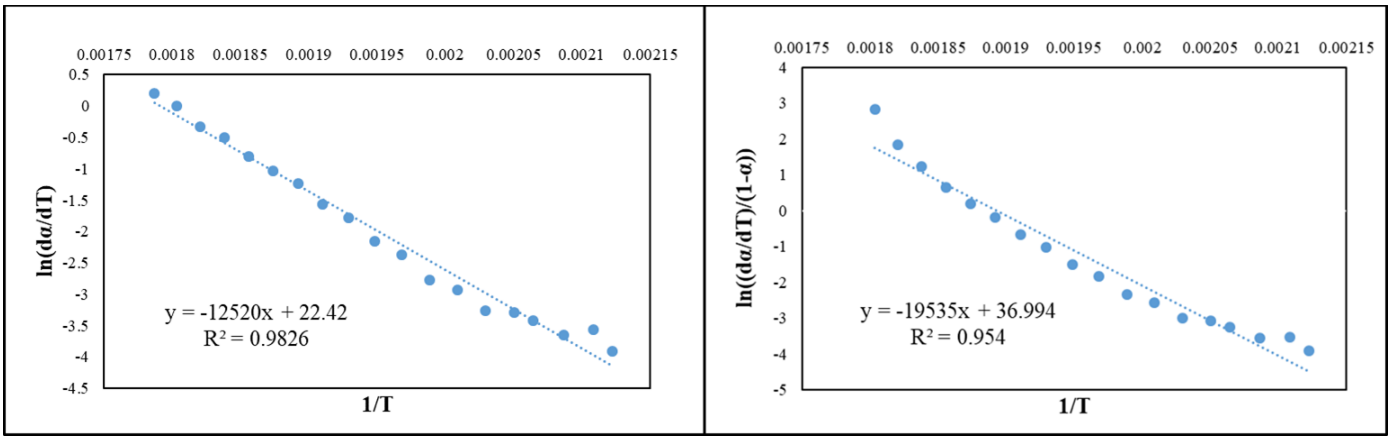

Figure 3: Arrhenius Linearization, Zero and First-Order Kinetics

c) Fitted Order

Multiple linear regression was applied to Equation (7) to get a linear relationship between the variables. The resulting equation had an R-Squared value of 0.9951

$$y = -9874.3\, x_1 - 1.347\, x_2 + 36.994 \qquad (17)$$

The values of the order of the reaction, pre-exponential factor and the activation energy in this case were found to be -1.347, 2.26×10^7 min^{-1}, and 82.09 kJ/mol respectively.

Estimation of the TMR_{ad} and the T_{D24}

The TMR_{ad} and T_{D24} results obtained from the analysis of calorimetric data using different mathematical methods are tabulated in Tables 1 and 2 below. All methods predicted a TMR_{ad} value that fell in the range of 11-14 minutes. The Enhanced Fisher's Method with the assumption of first-order kinetics gave the most conservative result of 11.61 minutes for the TMR_{ad}.

Table 1: TMR_{ad} Results for DMSO Phenol System (5 to 1 Molar Ratio)

Sl. No.	Method Used	TMR_{ad} at T_{on} (min)	Experimental TMR (min)

1.	Frank-Kamenetskii Method		12.02	12.20
2.	Integral Equation Derived From Rate Law (Equation 7)	Zero Order	13.55	
		First Order	12.76	
		n = -1.347	12.09	
3.	Enhanced Fisher's Method	Zero Order	12.04	
		First Order	11.61	
		n = -1.347	12.21	

The methods used to determine the T_{D24} gave values that fell in the range 120-144℃. The Model Based Estimation Method gave the most conservative value of 83.25℃. For the assumption of first-order kinetics, Equation (7) predicted a value of 142.63℃ which falls within 0.5% of the value predicted by the AKTS Thermal Safety Software, 143.20℃. The other results for the T_{D24} were comparable and fell within the range of 120-124℃.

Table 2: T_{D24} Results for DMSO Phenol System (5 to 1 Molar Ratio)

Sl. No.	**Method Used**		**T_{D24} (℃)**
1.	Frank-Kamenetskii Method		121.80
2.	Integral Equation Derived From Rate Law (Equation 7)	Zero Order	123.49
		First Order	142.63
		n = -1.347	120.68
3.	AKTS Thermal Safety Software		143.20
4.	Model Based Estimation Method		83.25

Simulation of Adiabatic Conditions

Equations 4 through 6 were used to reconstruct the Self-Heat Rate curve under purely adiabatic conditions for each of the three cases (zero-order, first-order and fitted-order kinetics).

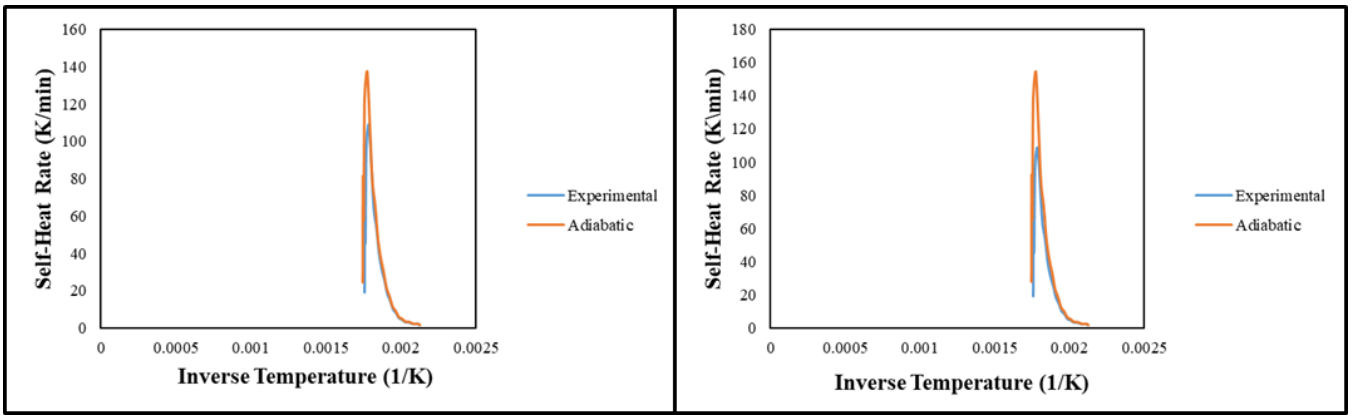

Figure 4: Experimental and Adiabatic Self-Heat Rate Curves for Zero and First-Order Kinetics

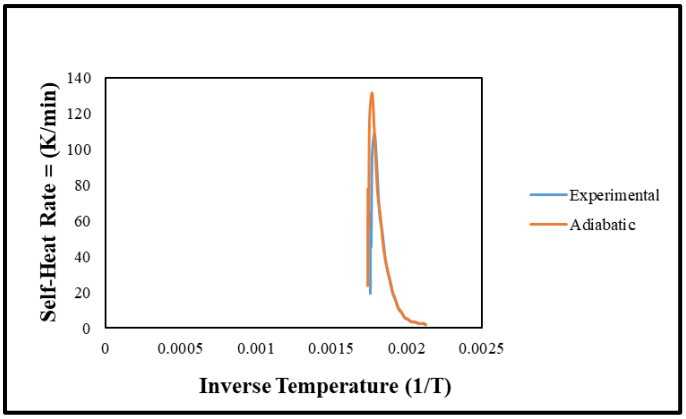

Figure 5: Experimental and Adiabatic Self-Heat Rate Curves for Fitted-Order Kinetics

Experimental Validation

An isothermal hold experiment was conducted on 10 ml of a sample containing DMSO and Phenol (5 to 1 molar ratio) using the ARSST. The sample was held at a temperature of 146℃ for a period of 24 hours. No rise in temperature was observed and a runaway reaction did not occur. However, a reaction did seem to have taken place and a black solid mass that smelt strongly of methyl mercaptan was observed.

Consolidated Results for All Systems

In the figure below (Figure 6), the values of T_{D24} calculated for different assumptions of reaction orders and using different methods are plotted as a function of the onset temperature. As expected, the values for T_{D24} predicted by the Frank-Kamenetskii Method and using Equation (12) more or less overlap because both methods assume the reaction follows zero-order kinetics. In the industry, 100 K and 50 K rules are commonly used to determine a safe operating temperature for exothermic processes. These rules state that at a temperature which is 100 K or 50 K below the onset temperature detected by a calorimeter, an exothermic process can be run safely. All the T_{D24} values calculated based on the zero-order assumption fall below the 50 K line. Some of these values fall on or very close to the 100 K line and the line representing the Model Based Estimation Method.

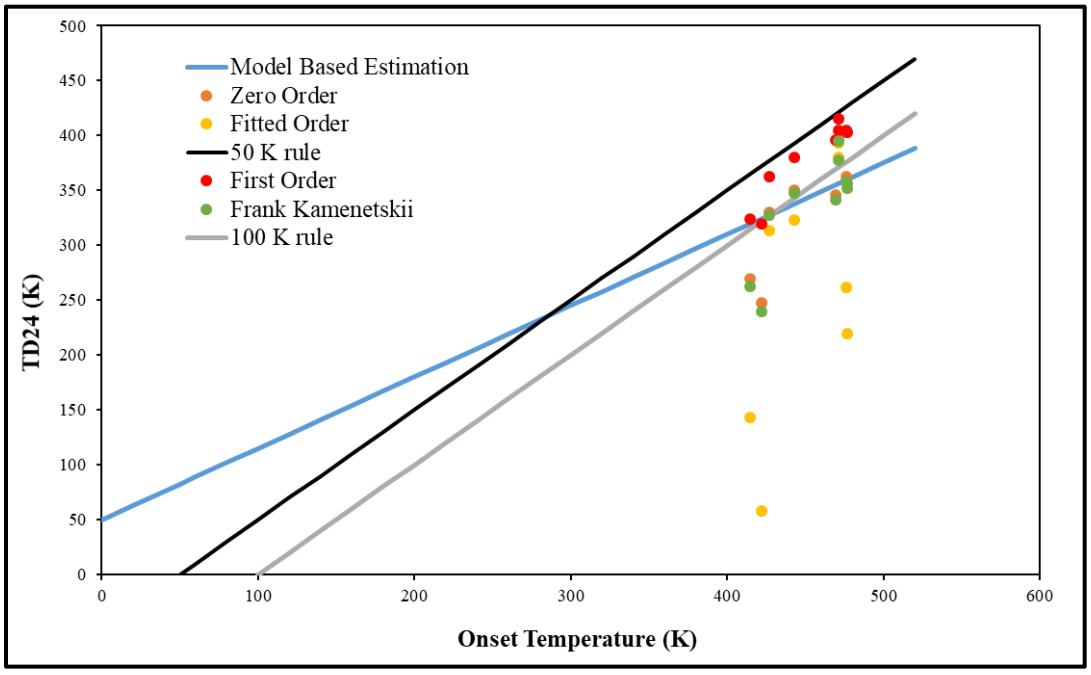

Figure 6: Calculated T_{D24} Values Plotted Against Corresponding Onset Temperatures

The values of T_{D24} calculated based on fitted-order kinetics using Equation (10) were found to be the most conservative with most points falling below the 100 K line and the Model Based Estimation Method. T_{D24} values predicted based on the assumption that reaction obeyed first-order

kinetics using the Equation (10) were less conservative but all points fell more or less between the 100 K and 50 K lines.

Table 3 below summarizes the TMR_{ad} and T_{D24} results obtained for all the systems that were considered for the purpose of this project. The calculated values of TMR_{ad} were found to be pretty close to experimental values of the 'Time to Maximum Rate'. On simulating purely adiabatic conditions using the Enhanced Fisher's Method, it was found that the Self-Heat Rate Curves were steeper and their peaks were longer (see Figures 4 and 5). This was true for all systems.

Table 3: Summary of Results for All Systems

System	Method Used		TMR_{ad} (min)	T_{D24}(°C)	Experimental TMR (min)
Pure DMSO (Data Set 1)	Frank-Kamenetskii Method		24.43	79.30	24.51
	Integral Equation 7	n = 0	25.34	83.49	
		n = 1	26	129.83	
		n = -0.614	26.14	-53.65	
	Enhanced Fisher's Method	n = 0	24.64	-	
		n = 1	23.31		
		n = -0.614	25.62		
	Model Based Estimation Method		-	86.86	
Pure DMSO (Data Set 2)	Frank-Kamenetskii Method		24.32	85.56	25.00
	Integral Equation 7	n = 0	25.59	89.44	
		n = 1	25.98	132.09	
		n = -1.685	17.72	-11.5	
	Enhanced Fisher's Method	n = 0	25.09	-	
		n = 1	23.76		
		n = -1.685	26.20		
	Model Based Estimation Method		-	86.56	
DMSO Acetic	Frank-Kamenetskii Method		15.52	74.79	
	Integral Equation 7	n = 0	16.74	77.13	
		n = 1	15.52	107.32	
		n = -1.551	13.22	49.8	

Acid (9 to 1 molar ratio)	Enhanced Fisher's Method	n = 0	15.83	-	15.86
		n = 1	15.16		
		n = -1.551	16.27		
	Model Based Estimation Method		-	64.76	
DMSO Acetic Acid (5 to 1 molar ratio)	Frank-Kamenetskii Method		18.81	54.00	19.66
	Integral Equation 7	n = 0	20.68	56.86	
		n = 1	18.99	89.41	
		n = -1.445	15.79	39.96	
	Enhanced Fisher's Method	n = 0	19.62	-	
		n = 1	18.76		
		n = -1.445	20.04		
	Model Based Estimation Method		-	54.68	
DMSO Phenol (9 to 1 molar ratio)	Frank-Kamenetskii Method		9.11	104.57	8.36
	Integral Equation 7	n = 0	10.27	106.58	
		n = 1	9.84	132.06	
		n = -1.226	8.41	106.79	
	Enhanced Fisher's Method	n = 0	8.27	-	
		n = 1	7.95		
		n = -1.226	8.35		
	Model Based Estimation Method		-	83.36	
DMSO Phenol (5 to 1 molar ratio)	Frank-Kamenetskii Method		12.02	121.80	12.20
	Integral Equation 7	n = 0	13.55	123.49	
		n = 1	12.76	142.63	
		n = -1.347	12.09	120.68	
	Enhanced Fisher's Method	n = 0	12.04	-	
		n = 1	11.61		
		n = -1.347	12.21		
	Model Based Estimation Method		-	83.25	
DMSO Methanol (9 to 1 molar ratio)	Frank-Kamenetskii Method		41.00	-10.53	44.20
	Integral Equation 7	n = 0	45.73	-3.69	
		n = 1	47.16	51.25	
		n = -0.565	47.15	-130	
	Enhanced Fisher's Method	n = 0	44.40	-	
		n = 1	42.32		
		n = -0.565	45.80		
	Model Based Estimation Method		-	46.47	
DMSO	Frank-Kamenetskii Method		43.72	-33.74	
		n = 0	42.54	-25.34	

Methanol (5 to 1 molar ratio)	Integral Equation 7	n = 1	37.67	46.92	42.67
		n = -0.456	47.22	-214.85	
	Enhanced Fisher's Method	n = 0	43.23	-	
		n = 1	41.09		
		n = -0.456	44.46		
	Model Based Estimation Method		-	51.25	
DMSO Water (9 to 1 molar ratio)	Frank-Kamenetskii Method		25.68	68.87	25.61
	Integral Equation 7	n = 0	25.66	73.13	
		n = 1	28.86	122.60	
	Enhanced Fisher's Method	n = 0	25.79	-	
		n = 1	24.51		
		n = -0.863	27.14		
	Model Based Estimation Method		-	82.26	

DISCUSSION AND CONCLUSIONS

Mathematical methods assuming lower orders of reaction result in more conservative values of the T_{D24}. The Frank-Kamenetskii Method and Equation (10) for the zero-order assumption resulted in approximately the same values of the T_{D24}. The reason behind observing this trend is the fact that lower reaction orders neglect the reduction in the rate of reaction due to the consumption of the reactant. The rate is assumed to increase exponentially with the rise in temperature and therefore, all the extrapolated results are conservative estimates. From a process safety perspective, these cases represent 'worst-case scenarios'.

The assumption that the reaction follows first-order kinetics resulted in slightly less conservative values. However, the T_{D24} value predicted for the first-order assumption (DMSO Phenol 5 to 1 molar ratio system) matched very closely with the value predicted by the AKTS Thermal Safety Software. The isothermal hold experiment that was run on the ARSST using a sample of DMSO and Phenol (5 to 1 molar ratio) couldn't validate the T_{D24} result obtained. We believe that the

amount of sample used for the experiment was too small to have released enough heat in order to cause a detectable change in temperature. The ARSST has a sensitivity of 0.1℃/min, which could also be a contributing factor. The Accelerating Rate Calorimeter (ARC) on the other hand, has a sensitivity of 0.02℃/min. However, the ARC has a higher ϕ-factor.

Simulation of adiabatic conditions using the Enhanced Fisher's Method showed that under purely adiabatic conditions, the rate at which temperature increased would be higher and the resulting temperatures would be higher as well. The difference between the simulated self-heat rate curve and the experimental self-heat rate curve however, was not too significant because the ARSST is a pseudo-adiabatic calorimeter with a low ϕ-factor (≈1.05).

On applying multiple linear regression to the Arrhenius Linearization Equation, the calculated values for the orders of the reaction for all DMSO systems were found to be negative. This indicates that the decomposition reaction is probably autocatalytic and/or multi-stage.

The calculated values of the TMR_{ad} were largely dependent on the kinetics parameters, k_o and E. Therefore, their values fell within a small range of the TMR under experimental conditions.

PROPOSED STEPS FORWARD

Adiabatic experiments can be run on the ARSST for the different DMSO systems at calculated values of the T_{D24} to see if a runaway reaction actually occurs at that temperature. This would experimentally validate the mathematical methods used for the purpose of this project. If a runaway reaction is not observed, adiabatic experiments can be run at calculated values of the T_{D8} (temperature at which the TMR_{ad} is 8 hours) instead.

DSC experiments can be conducted for the different DMSO systems and this data can be fed to the AKTS Thermal Safety Software to predict the value of the T_{D24}. The results can then be compared with the T_{D24} values calculated using the mathematical methods described in this report.

Since results for the kinetics of the reactions have been obtained, we can attempt to simulate isothermal DSC data. The results of simulation can then be compared with results from actual isothermal DSC experiments.

We had concluded that the decomposition of DMSO is probably autocatalytic. Therefore, it would make sense to model the kinetics of the reaction based on the assumption that the reaction is autocatalytic.

In the future, we could also extend the scope of the project to different compounds, preferably APIs (Active Pharmaceutical Ingredients) that are of importance to the pharmaceutical industry. The main incentive behind this project was the fact that the 100 K and 50 K rules can be too restrictive for lower onset temperatures and the T_{D24} would provide a more scientifically accurate solution in such cases (because it is based on reaction kinetics). Therefore, future steps must be taken in this direction.

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