CHAPTER IV
EXPERIMENTAL

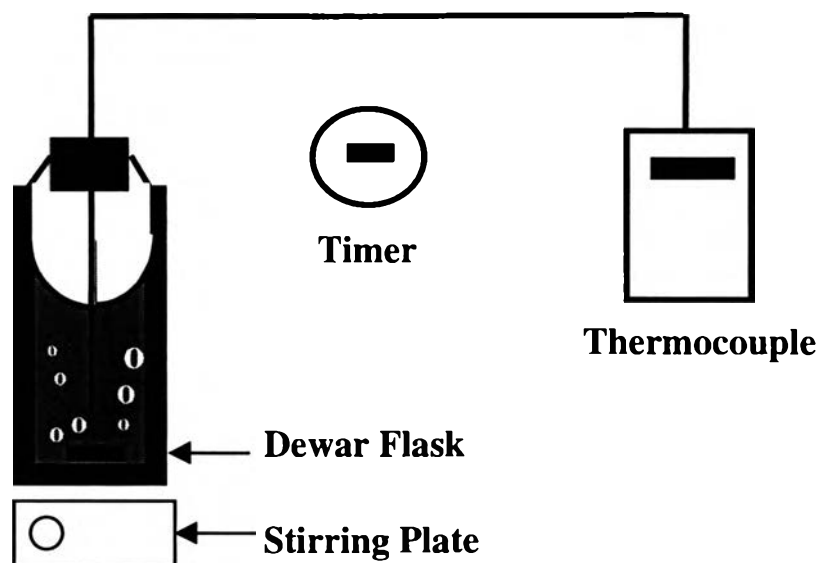## 4.1. Reaction Kinetics

4.1.1 Materials

Sodium nitrite ($NaNO_2$) and ammonium chloride (NH_4Cl) purchased from Aldrich were used as oxidizing and reducing agents, respectively. Hydrochloric acid HCl 98% was used to reduce the pH while sodium hydroxide (NaOH) was used to increase the pH of the solution; both chemicals were purchased from Aldrich. All chemicals used were of reagent grade.

4.1.2 Kinetics Study

The kinetics of this reaction was investigated using a batch reactor (Dewar flask, Fisher, U.S.) which can be considered adiabatic for a short initial period of the reaction. Temperature and pH of the solution were monitored using a digital thermometer with a type J thermocouple and a pH meter purchased from Cole Palmer, U.S. The schematic of the experimental setup is shown in Figure 4.1. Initial rate method was applied to find the order of the reaction as well as the rate constant expression. To find the reaction order with respect to each reactant, the concentration of one reactant was held constant at a higher concentration, while the other reactant's concentration was varied. To determine the rate constant expression, the pH was held constant using different amounts of hydrochloric acid or sodium hydroxide, while the initial temperature was varied. The temperature-time profiles obtained were then manipulated using equations (3.11) to (3.16) to find the reaction orders, the rate constants and the activation energies.

Figure 4.1 Schematic of the adiabatic batch reactor setup for reaction kinetics study.

4.2. Polymer Dissolution Kinetics

4.2.1. Materials

Hard gelatin capsules (0CS, 4CS - natural/transparent) were purchased from Capsugel^{TM}. Eudragit® S100 (Rhöm Pharm, Dramstadt, Germany) obtained through RohmAmerica was used as a coating polymer which is soluble in the reactive system (aqueous medium) in the working pH range (5 to 8). Ethanol and acetone used as solvents to prepare polymer solution were purchased from Aldrich. Sodium nitrite ($NaNO_2$) and ammonium chloride (NH_4Cl) also purchased from Aldrich were used as the oxidizing and reducing agents, respectively. Citric acid $C_6H_8O_7$ was used as a pH-reducing agent (catalyst) while sodium hydroxide (NaOH) pellets were used as a pH-adjusting agent. Both chemicals were also purchased from Aldrich, U.S. All chemicals and solvents used were of reagent grade.

4.2.2. Preparation of Catalyst-filled Capsules

The 18 wt % polymer solution used for coating capsules was prepared by stirring 17.27 g Eudragit® S100 pellets in a mixture of 40 ml Ethanol and 60 ml Acetone for about one hour until achieving a clear solution. Hard gelatin capsules were filled with 0.001 mole (0.192 g) citric acid. After being locked,
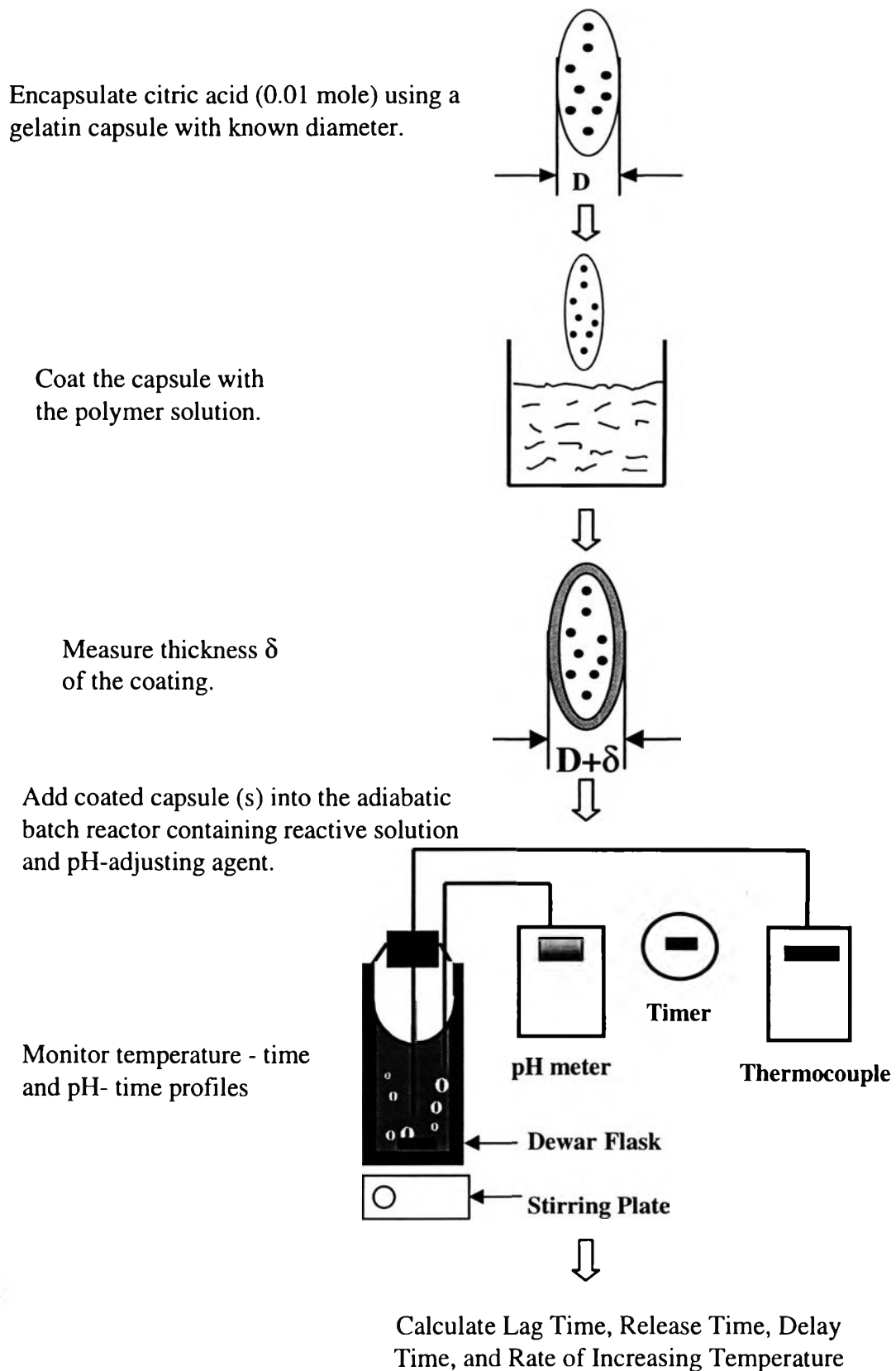
the core capsules obtained were coated with the polymer solution by means of alternatively dipping half of the capsule into the polymer solution, then drying it until almost all the solvents were evaporated (about half a day). The procedure was then repeated for the other half of the capsule. The thickness of the polymeric coat was varied by changing the number of dipping and drying times.

4.2.3. Measurement of the Coating Thickness

Thickness of each capsule before and after being coated were measured using a dial gauge (SIS-6 from Peacock, Japan). The dial gauge can measure a thickness to the accuracy of $\pm$ 0.01 mm; however, the precision of measuring thickness by that gauge was found to be in the order of $\pm$ 0.03 mm. Therefore, in calculating experimental error for measuring coating thickness, $\pm$ 0.03 mm was used as the variation. Thickness of the Eudragit®S - coated layer was then deduced from the difference of the two thickness. Four different positions were measured for each capsule to calculate the least thickness difference.

4.2.4. Polymer Dissolution Kinetics Study

To determine the kinetics of polymer dissolution as well as to obtain parameters not only for evaluating the efficiency of the encapsulation technique but also for the comparison of experimental and simulated results, experiments were conducted in a batch reactor. Temperature-time and pH-time profiles were recorded for each experiment. The experimental plan is shown in Figure 4.2. Effects of stirring speed, thickness of the polymeric coat, initial temperature, initial pH of the solution, and number of capsules used per unit volume of the reactive solution were studied. All important experiments were carried out in duplicate.

Encapsulate citric acid (0.01 mole) using a
gelatin capsule with known diameter.

Coat the capsule with
the polymer solution.

Measure thickness δ
of the coating.

Add coated capsule (s) into the adiabatic
batch reactor containing reactive solution
and pH-adjusting agent.

Monitor temperature - time
and pH- time profiles

Timer

pH meter

Thermocouple

Dewar Flask

Stirring Plate

Calculate Lag Time, Release Time, Delay
Time, and Rate of Increasing Temperature

**Figure 4.2 Experimental setup for polymer dissolution kinetics and fused
chemical reaction studies.**

From the pH-time profiles monitored, values of the lag time and the release time were deduced and used in the polymer dissolution kinetics study while from the temperature-time profiles, values of the delay time and the rate of increasing temperature were computed for the verification of the simulated results. Methods to obtain those parameters are shown in Figure 4.3. Essentially, the lag time is the time when the pH of the solution begins to drop due to the release of the catalyst inside the capsules, or in other words, that is the time when the polymeric coat and the gelatin capsule have been dissolved. The release time is computed from the lag time to the time when the pH of the solution stabilizes. Regarding the parameters obtained from temperature-time profiles, the delay time basically gives us an idea as to when the temperature starts shooting up while the rate of increasing temperature describes how rapidly the temperature shoots up after the delay time.
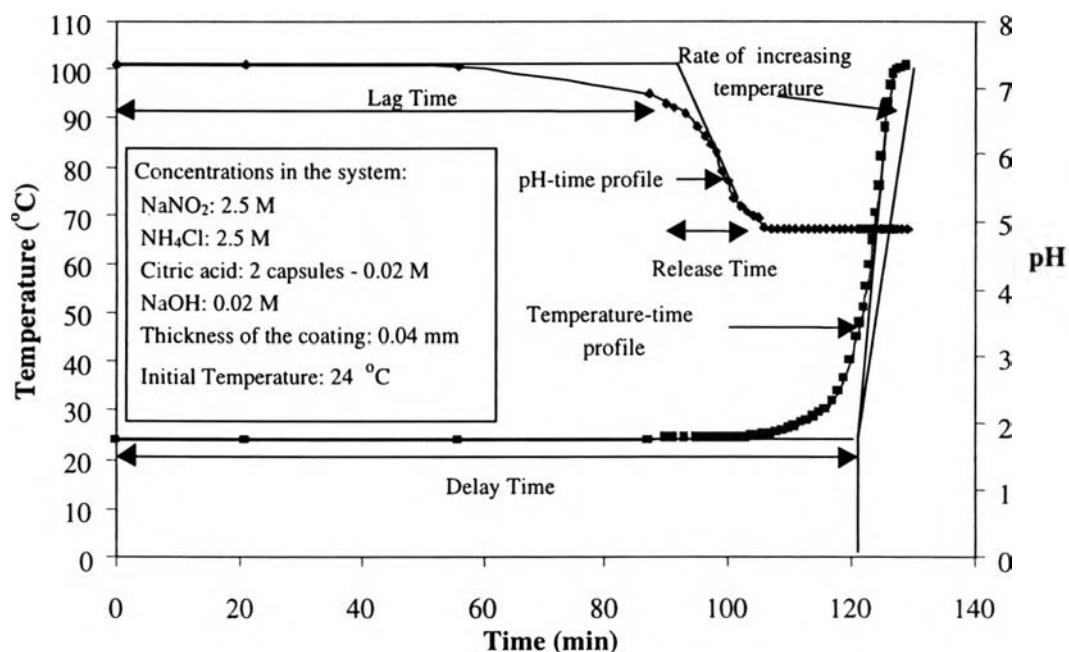
Figure 4.3 Definition of parameters deduced from the temperature-time and pH-time profiles.