Chapter 2

AIMS AND OBJECTIVES
2.1 Aims and objectives

The aim of this thesis was to develop new analytical methodologies for the estimation of monomers to address certain important issues related to industrial production of poly(lactic acid) and polymerisation processes that include acrylic and styrenic HIPEs.

Chapter 1 outlined the importance of analytical chemistry, analytical perspective - analytical approach to solving problems in various fields of chemistry. It also outlined how chromatographic techniques could be efficiently used to carry out analysis of various analytes in complex matrices. It summarised about the availability of various chromatographic techniques with the options of a wide range of stationary phases and detection systems available today.

As in all scientific research, a rational systematic approach is essential for solving problems related to analytical method development. This requires a sound knowledge of chemical and physical sciences for thorough understanding of analytical instrumentation, accurate judgement of analyte behaviour and an active approach to address possible technical and chemical analytical pitfalls. While developing analytical methodologies for generating meaningful data, analytical chemist has to overcome challenges which demand working with smaller samples, with more complex materials/matrices, with processes occurring on shorter time scales, and with components present at lower concentrations. While addressing specific needs of a particular problem, an analytical chemist has to choose the right analytical technique, configure components of instrument appropriately and optimise various parameters to suit typical analysis requirements. This process is called analytical method development.
Each analysis problem chosen in the present study is unique in terms of requirement and complexity of the analysis which demands choosing an appropriate chromatographic technique and configuration of equipment, developing sample preparation technique and optimising other parameters of analysis accordingly.

Once analytical method is developed, it needs to be validated to demonstrate that the proposed method is suitable for its intended purpose. The present work was also aimed to perform method validation for all the analytical methods developed in this work. Validated analytical data are used for the evaluation of original investigations, medical diagnosis, environmental assessment, purity estimation for important chemicals and other varied purposes. In this context, method validation has received considerable attention in literature and from industrial committees and regulatory agencies.

The objectives of this thesis were to develop analytical methodologies for:

- Estimation of chemical purity of lactic acid monomer by impurity profiling.
- Estimation of optical purity of lactic acid.
- Measurement of 2-ethylhexyl acrylate (EHA), ethylene dimethacrylate (EGDMA) and 2-ethylhexyl methacrylate (EHMA) for estimating monomer conversions in HIPE polymerisation reactions.
- Measurement of trace levels of EHA, EGDMA and EHMA in HIPE process water.
- Measurement of styrene, divinyl benzene (DVB) and EHA for estimating monomer conversions in HIPE polymerisation reactions.
The chapter-wise summary of objectives and the significance of present work are given below.

2.1.1 Estimation of chemical purity of lactic acid monomer

Lactic acid produced by fermentation process contains carboxylic acid impurities which are detrimental to the polymerisation ability of lactic acid resulting in low molar mass PLA, which is not useful for most applications. PLA of high molecular weight is needed to produce devices of high mechanical strength. Evaluation of chemical purity of lactic acid monomer (in terms of carboxylic acid impurities) is therefore an important parameter in PLA production.

Chapter 3 deals with the establishment of a suitable analytical method for the impurity profiling of lactic acid monomer. An analytical method based on polar-embedded reverse phase HPLC was developed and various carboxylic acid impurities in lactic acid samples were identified and quantified. The other components present in lactic acid, the PLA precursors, viz. lactoyl lactic acid and the cyclic dimer (3,6-dimethyl-\(p\)-dioxane-2,5-dione, also called as dilactide) were identified by indirect method (by monitoring changes in peak heights of dilactide and lactoyl lactic acid on hydrolysis of lactic acid sample).

A separate GC method was also developed to measure ethanol and methanol, the byproducts of hydrolysis of lactic acid ester, which may appear as impurities in final product, if not completely removed in reactive distillation step of its downstream purification.
A thorough method validation was performed by investigating system precision, specificity, linearity (calibration studies), limits of detection and quantification, ruggedness of method, ‘method precision and accuracy’, and ‘Gauge R & R’ study.

2.1.2 Estimation of optical purity of lactic acid monomer

The small amounts of enantiomeric impurities drastically change properties such as crystallinity or biodegradation rate of the polymer. L (+) lactic acid is required for production of PLA suitable for most applications. Therefore, besides evaluation of chemical purity, estimation of optical purity of lactic acid monomer is also a crucial factor in deciding physical properties of PLA.

Chapter 4 deals with the establishment of an analytical method for estimation of optical purity of lactic acid monomer. The HPLC method based on CLEC (chiral ligand exchange chromatography) was developed for the separation of lactic acid enantiomers. In this work, enantiomeric separation of lactic acid was accomplished by employing stationary phase ligand, which employs L-hydroxy proline as the immobilised chiral selector. The chromatographic parameters such as column temperature, flow rate, detection wavelength and solvent composition were investigated and optimised to achieve separation of lactic acid enantiomers. System precision was investigated by studying repeatability of retention times and peak area. The method was applied to estimate the optical purity of lactic acid synthesised in our laboratory as well as commercial ones.

2.1.3 Estimation of monomers in acrylic HIPEs

Synthesis of PolyHIPE materials using HIPE methodology has gained considerable commercial interest in recent years. Acrylic monomers, viz. EHA, EGDMA
and EHMA are used to produce Functional Absorbent Materials (FAM) using HIPE polymerisation. Studying the rate of monomer conversion (reaction kinetics) is important for process optimisation. This necessitates development of an analytical method, which can estimate time-dependent monomer conversions by analysis of unreacted monomers (EHA, EGDMA and EHMA) in HIPE polymerisation reactions.

Part A of chapter 5 deals with the establishment of an analytical method for measurement of EHA, EGDMA and EHMA in high internal phase emulsions. For this, an analytical method based on gas chromatography (GC), employing flame ionisation detector, was developed and its application was demonstrated by estimating monomer conversions in acrylic HIPE polymerisation under certain selected reaction parameters. The chromatographic system was configured and the protocol for extracting monomers from high internal phase emulsion, sample preparation technique and GC column oven temperature programming were developed and optimised. Method validation was carried out by investigating system precision, specificity, linearity, limit of detection (LOD), limit of quantification (LOQ), ‘method precision and accuracy’, and Gauge R & R.

Part B of chapter 5 deals with the establishment of sensitive HPLC-UV method, which can estimate EHA, EGDMA and EHMA at low ppm levels in HIPE process water. The HIPE process water samples were generated in laboratory and investigated for contents of residual monomers at trace levels. This method is useful to assess the quality of process water (in terms of residual monomers) before being recycled in industrial process pertaining to production of Functional Absorbent Materials (FAM) using HIPE methodology.
The reverse phase (RP)-HPLC method was employed for achieving chromatographic separations. The chromatographic conditions like mobile phase composition, flow rate and the detection wavelength were optimised and complete baseline separation of analytes was achieved. The method was established by performing method validation, which included investigation of system precision, specificity, linearity, response factors, limit of detection, limit of quantification, and ‘method precision and accuracy’.

2.1.4 Estimation of monomers in styrenic HIPEs

Chapter 6 deals with the establishment of an analytical method for estimation of monomer conversions in styrenic HIPE polymerisation. The monomers selected for styrenic HIPE system were styrene, DVB and EHA. The procedure for extraction of monomers from high internal phase emulsion was developed and validated. The sample preparation technique and GC column oven temperature programming were developed and optimised for achieving complete baseline separation of analytes. Method validation was carried out by investigating system precision, specificity, linearity, limit of detection (LOD), limit of quantification (LOQ), ‘method precision and accuracy’. A Gauge R & R study was conducted to assess the performance of method. The usefulness of method was demonstrated by estimating monomer conversions for HIPE polymerisation reactions that used thermal and redox initiator systems.

The thermal initiators used in this work included sodium persulphate and cumene hydroperoxide; and redox initiator systems included “sodium persulphate: sodium dithionite”, “sodium persulphate : ascorbic acid”, “cumene hydroperoxide : ascorbic acid”, all used in 1:1 molar proportion.