Summary of the Thesis

The thesis concerns with the isolation and characterization of less known (2S,3S)- and (2S,3R)-tetrahydro-3-hydroxy-5-oxo-2,3-furan dicarboxylic acids obtained from locally available plant materials. Exploration of the molecules for using in the broad areas of chirality have been attempted.

A systematic literature search has been carried out on naturally occurring chiral acids (excluding amino acids) which have found application in the broad area of asymmetric synthesis. It is revealed that though there are several chiral hydroxy acids which are known to involve in various aspects of chirality very little is known about the title acids. Though several reports pertaining to the pharmaceutical applications are available, especially in fat metabolism and also as anti-obesity agents, the chemistry of these diastereomers still remains unexplored in spite of the fact that these compounds can be easily made available from cheap natural sources. In fact these acids endowed with unique stereo structure have evaded the attention of organic chemists. Hence it is the objective of the present study to explore the possibility of using these acids as chiral agents namely catalyst, ligand, liquid crystal dopant and chiral selector in the liquid chromatographic separation.

Towards the search for inexpensive chiral molecules possessing numerous functional groups and stereocenters for employing them in the synthesis of enantiomerically pure compounds diastereomeric (2S,3S) and (2S,3R)-tetrahydro-3-hydroxy-5-oxo-2,3-furan dicarboxylic acids have been identified. Efficient practical green isolation methods have been developed for the large scale isolation of the same from renewable resources.

As the Vibrational Circular Dichorism (VCD) has emerged as an important tool for the determination of absolute configuration and enantiomeric purity of optically active molecules in the solution state the optical integrity of the title molecules has been verified by a systematic VCD analysis. The conformer populations of the molecules were generated with MMFF calculations which showed that the acid carbonyl groups would
distort the carbonyl peak in the IR and VCD spectra. As expected a sharp band for the IR and a broad band for the VCD were observed. An attempt was made to average the IR spectra of the conformers and is compared with the VCD spectra. The spectral phases match well with the calculated spectra and thus confirms that the Garcinia acid has (2S,3S) and Hibiscus acid has (2S,3R) absolute configurations respectively.

The Dialkyl (2S,3S) and (2S,3R)-tetrahydro-3-hydroxy-5-oxo-2,3-furandicarboxylates of the acids were prepared for exploring them as chiral catalysts in the asymmetric reductions of ketones.

It is expected that a chiral (acyloxy) borane (CAB) complex is formed in situ while mixing sodium borohydride and the title acids in THF at 0°C. These two structurally different intermediates formed from the title acids are responsible for the formation of the reduced products from the ketones in varying enantiomeric excess. Tentative mechanisms have also been proposed for the chiral discrimination of the ketones.

Enantiomerically pure1,2-diols and related substrates play significant role as chiral synthons in the syntheses of natural and biologically active molecules. Having two centers of chirality and vicinal diol moiety, trialkyl esters of (2S,3S)- and (2S,3R)-tetrahydro-3-hydroxy-5-oxo-2,3-furandicarboxylic acids are expected to find extensive application in asymmetric reactions especially as chiral agents.

Novel triols namely (4S,5S)-4-(2-Hydroxy-2,2-diphenyl ethyl)-2,2-Dimethyl-α,α,α’,α’-teta aryl-1,3-dioxolane-4,5-dimethanol and (4S,5S)-4-(2-Hydroxy-2,2-di(1-naphthyl)ethyl)-2,2-Dimethyl-α,α,α’,α’-teta aryl-1,3-dioxolane-4,5-dimethanol have been prepared from (2S,3S)-tetrahydro-3-hydroxy-5-oxo-2,3-furan dicarboxylic acid. These triols have been effectively converted to chiral titanium complexes and subsequently employed as chiral ligands in asymmetric Diels-Alder reaction involving cyclopentadiene and 3- crotonyl oxazolidinone. The optically active endo Diels-Alder adduct, namely 1-[(3-methyl bicyclo[2.2.1] hept-5-ene-2-yl) carbonyl]-2-pyrrolidinone is isolated. The optical activity of these product clearly indicate the potential of (2S,3S) and (2S,3R)-tetrahydro-3-hydroxy-5-oxo-2,3-furan dicarboxylic acids as chiral catalyst in asymmetric Diels-Alder reactions.

A new silica gel based Chiral Stationary Phase, Poly-AVTFC, has been developed from (2S,3S)-tetrahydro-3-hydroxy-5-oxo-2,3-furan dicarboxylic acid for the liquid chromatographic separation of enantiomers. The anhydride namely (6-
aS)-2,4,6-trioxo tetrahydrofuro[3,4-b] furan-3(4H)-yl-acetylate obtained from the acid has been condensed with 4- Vinyl aniline to get the monomer, (2S,3S)-3 -(Acetyloxy) -5-oxo-2-[ 4-Vinyl anilino carbonyl ] tetrahydro-3- furan carboxylic acid, AVTFCA in good yield. The monomer on subsequent polymerization reaction with silica gel functionalized with dichloride of 4,4'-azo-bis-cyanovaleric acid to yield the subject Chiral Stationary Phase. Attempts have been made for the Liquid chromatographic separation of various racemic compounds and it is found that racemic α-methyl benzyl amine has been resolved in heptane - ethyl acetate solvent system.

Attempts were also made to synthesize (4S,5R)-4- [[3,- (1,3) –dithain-2-yliden)-1-pyrrolidinyl] carbonyl]-4-hydroxy-5-methyldihydro-2-(3H), furanone, an analog of pyrrolizidine alkaloid and Dimethyl (2S,3S) and (2S,3R)- 3- ( acryloxy )-5-oxo-tetrahydro-2,3 furandicarboxylate, a dienophile from the title acids, for Diels- Alder reaction.