PREFACE

India is not excluded from the problems encountered worldwide in the treatment of nosocomial urinary tract infections, commonly caused by enzyme-producing Enterobacteriaceae (Abigail and Dixie, 2005). These enzymes (beta lactamases and ESBLs) are capable of hydrolysing the β-lactam agents like Amoxicillin, Ceftriaxone, Cefuroxime, Ceftazime, etc. The production of Amp C and Metallo beta lactamases were demonstrated in majority amongst uropathogens (Singhal et al., 2005). Resistance to these antibiotics was readily transferred between strains mainly through plasmids.

Measures that are considered to overrule the problem of antibiotic resistance include molecular level study of pathogens, manipulating drug therapeutics and kinetics. The imperative possible strategy towards solving problem of antibiotic resistance is the rational localization of bioactive phytochemicals. A number of these agents appear to have structures and modes of action that are distinct from those of the antibiotics in current use, suggesting that cross-resistance with agents already in use may be minimal (Rao et al., 2006; Verschueren, 1993).

In the present investigation work has been carried out in two phases. 76 nonrepetative clinical isolates were isolated and identified using conventional methods. These clinical isolates were identified for their geographical and gender based epidemiology, resistotyped as per CLSI recommendations and screened for higher degree of drug resistance. The age group 20-30, of females was found to be most susceptible to the infection. E. coli is found to be the major etiological agent for UTI. The antibiotics like Ampicillin (95%),
Ciprofloxacin (93%), Methicillin, Carbencillin (76%), Pipracillin (63%), etc. showed higher degree of resistance. Fifteen *E. coli* isolates showing multiple drug resistance were further selected and studied with respect to various molecular and functional aspects which contribute for their virulence, atypicalness and multiple antibiotic resistant nature especially for beta lactam antibiotics by production of Extended Spectrum Beta Lactamases i.e. ESBLs (Al-Jassar 2006). The percentage occurrence of Serum resistance, Heamagglutination and Cell surface hydrophobicity was observed in maximum strains of selected *E.coli* while the detection of Colicin production, Haemoglobin proteases production and hemolysin production was moderately observed. Atypical biochemical characters studied are production of H$_2$S, Urease activity, Citrate utilization, Adonitol utilization, Dulcitol utilization and Raffinose utilization of isolates which was observed using indicator agar. Statistical analysis has shown co existence of Ser-Hl, Hae-HBp, Hae-CHS, Hl-Col, Hl-Ser, CSH-HBp and CSH-Hae with each other. Co existence of ESBL was observed with Hl (33%), CSH (41%), Col (41%), HBp (41%), Hae (58%) and serum resistance (41%).

The uropathogenic *E. coli* Y3 showing higher degree of atypicalness and majority of positive virulence factors was investigated for production, purification and characterization of beta lactamase enzyme. Nine herbs were used to evaluate their antimicrobial and enzyme inhibition activity amongst them *Termnilia chebula* was found to be the most effective enzyme inhibitor. The enzyme inhibition was found to effective towards water extract of *Termnilia chebula* amongst all extracts studied. The major inhibitory constituent in the extract was found to be containing Gallic acid as
per the Insilico analysis. Enzyme inhibition potential of various concentrations of crude extract with amoxicillin was tested against clinical isolate Y3.