 SUMMARY

Paediatric Urinary Tract Infection (UTI) became a serious threat to the health of human population due to its severity caused by various uropathogenic microorganisms and their virulence factors. Even though it is asymptomatic, it requires proper diagnosis and effective therapeutic measures to overcome it; otherwise it may lead to severe kidney damage also. Hence, periodic surveillance of this infection is an emerging problem all over the world not an exception to the rural population. Therefore the development, modifications or searching the antimicrobial phytocompounds having bactericidal potential against drug resistant bacteria is a priority area of research.

For the present study, total number of 4326 urine samples were collected from both male and female patients of rural population in and around Perundurai, Erode District, Tamilnadu, India, between the period of January 2009 and December 2011, of which 1026 samples were identified as significant bacteriuria {546 (53.22%) female patients and 480 (46.78%) male patients}. Identified predominant causative uropathogens (60.5% of \textit{E.coli}) and their urovirulence characteristics were determined. Among the various uropathogens, the prime \textit{Escherichia coli} were shown highest rate of resistance (98.6 %) to nalidixic acid followed by amoxycillin (92.5%) and norfloxacin (87.9 %) respectively. Based on the antibiotic susceptibility/resistance pattern of various antibiotics over the period of three years, Multiple Drug Resistance (MDR) among the uropathogenic bacteria were observed, in which one of the uropathogenic \textit{E.coli} isolate was subjected to molecular characterization analysis such as strain identification (KMS 1), 16s rRNA sequencing and phylogenetic tree construction.

To overcome the problem of drug resistance, herbal medicines became the wonderful therapeutic measure since time immortal. The literature survey and pharmacological activity based chosen medicinal plants for this research, viz. \textit{Coriandrum sativum} (seed), \textit{Terminalia chebula} (dry fruit), \textit{Allium sativum} (clove), \textit{Emblica officinalis} (fruit) and \textit{Curcuma longa} (dry rhizomes) were screened for its antibacterial activity against the Multiple Drug Resistant (MDR) uropathogenic \textit{E.coli}. In resulting of the high inhibitory potential in preliminary tests, \textit{Terminalia chebula} was selected for further study and its methanolic extract phytocompounds revealed subsequently by HPTLC analysis in which toluene: ethyl acetate: formic acid: methanol (4.3:4.3:1.2:0.3 v/v/v/v) was employed as mobile phase and the results shown that the Rf values of used standards such as Tannic acid (0.78), Gallic acid (0.74) and Ellagic acid (0.63)
respectively. Simultaneously, quantitative estimation of methanolic extract of *Terminalia chebula* showed the recovered quantity of Tannic acid, Gallic acid and Ellagic acid was found to be 16.13µg, 279.42 ng and 22.00 µg /3µl in partially purified methanol extract respectively. Based on the presence of bioactive phytocompounds in the methanol extract of *T.chebula*, they were auto docked with the virulence protein, α – haemolysin, of uropathogenic *E.coli*, an effective binding energy potential of the bioactive lead compounds, gallic acid – 4.28 kcal/mol; ellagic acid of – 6.12kcal/mol with various possible active targets of the virulence protein and ranked to identify the most suitable and the better target to predict their mode of action.

The green synthesized silver nanoparticles from *T.chebula* methanolic extract, their optimization and characterization were analyzed. The critical virulence factors of uropathogens bacterial adherence to mucosal surfaces and their biofilm formation were evaluated by congo red agar, tube adherence and micro titer plate assay methods and the results were interpreted. Biofilm inhibitory potential of methanol extract and its mediated silver nanoparticles from *T.chebula* against uropathogens was analyzed by using Confocal Laser Scanning Microscope (CLSM) and the results were interpreted as 30µg/ml of the methanol extract showed better biofilm inhibitory activity against the tested uropathogenic *E.coli* (KMS 1) strain. Since an understanding on the traditional medicinal plant’s antibacterial and anti - adherence mechanisms would allow physicians to develop appropriate strategies for UTI prevention and adequate management protocols. Hence, this first study undertaken to determine the biofilm inhibitory potential and antibacterial activity of *T.chebula* and their green synthesized silver nanoparticles could lead to develop a potential alternative phytotherapy against multidrug resistant uropathogenic *Escherichia coli* in a rural population of Erode district.

Future studies can be focused on to search the specific adherence mechanism of biofilm forming Multiple Drug Resistance Uropathogenic *E.coli* to the mucosal epithelial cells in the urinary tract. Biofilm formation can be achieved by the way of cell to cell communication by signals (quorum sensing) molecules. With the formulation and the discovery of novel therapeutic agents by the green synthesized silver nanoparticles, an inhibition of communication signals (quorum quenching) may be achieved in a systematic approach.