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WORLDWIDE SPREAD OF MDR BACTERIA SIGNALS TO BE RESIDENT OF GUT MICROBIOTA FOR VITAMIN SYNTHESIS AND HETEROGENEOUS PHYTO-ANTIBIOTICS MAY CURE MDR INFECTIONS GLOBALLY

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WHO advocates worldwide action plan promoting research on phyto-antibiotics, gene medicines and conventional anti-microbials to stop superbugs horror that claims million deaths due to ineffectiveness of antibiotics. WHO has also recommended controlled use of antibiotics in patients and bans use of excess antibiotics in agricultural land and food animal growth. Our study indicated that more than 40% of sea, river and rain water bacteria were resistant to semi-synthetic antibiotics like ampicillin and amoxicillin. *blaTEM, blaCTX-M, blaOXA* types beta-lactamases, *AacC1/A1* acetyl transferases and AphA4 phospho transferases including *catB3, sul1/2 and strA/B* genes were detected in most plasmids and certain MDR chromosome islands as in *E. coli, P. aeruginosa, K. pneumoniae, S. enterica, M. tuberculosis, S. aureus and A. baumannii*. Plasmids carrying blaNDM1 and blaKPC genes are increasing and wonder drug imipenem is becoming useless in few cases and Mcr-1 gene in E. coli plasmids has made colistin drug useless. *TetA/C, acrAB-TolC, mexAB/CD/EF-oprM, macAB, mtrCDE* drug efflux genes were activated causing many antibiotics (tetracycline, azithromycin, amikacin, norfloxacin) useless. *RpoB, pncA, ponA, penA, and rpsL* mutations are involved in multi-resistance in TB and gonorrhoea. *GyrA/B or parC* genes mutations and *aac6'-1b-cr* gene accumulation were the cause of widespread fluoroquinolones (ciprofloxacin) drug resistance mtrR, acrR, tetR and ampR types transcriptional regulators have also accumulated in superbug plasmids and are activated by antibiotics increasing superbug sepsis and death. PubMed and GenBank search indicated antimicrobial resistance (AMR) had created an acute problem in modern society worldwide and could be designated as 21st century pseudo antibiotic dark age. Abundant multi-drug resistant (MDR) bacteria from Kolkata Ganga River and Digha Sea were detected and characterized as Extended Spectrum Beta-Lactamases (ESBL) superbugs (*Escherichia, Phenalkaligenes, Pseudomonas, Streptococci, Citrobacter, and Stenotrophomonas*). AMR could be resembled to many hallmarks of cancer cells: MDR genes in plasmids similar to diversified oncogenes, active mutations producing ESBL and inhibitor resistant similar to GTP-bound Gly->Val mutant Ha-ras oncoprotein, activation of *blaCTX-M, acrAB, tetA and cmr* genes with high copy number and expression, similar to over expressed retroviral oncogenes and high amount of small plasmid-like DNAs apart from large conjugative plasmids similar to high copies of chromosomes and miRNA in tumour cells. However, we have forgotten that 2x1012 bacteria in the intestine are constantly synthesizing 20 vitamins and complex bio-molecules for our body and one high dose of antibiotics is enough to kill all such microbiota. Thus, it appears, multidrug-resistant genes creation is to protect microbiota from repeated doses of antibiotics that we have consumed since 1940s. Thus, MDR bacteria will be the resident of intestine favouring vitamin biosynthesis, needed for normal human metabolism. Several high-quality research from US Human Microbiome Project (HMP), European Metagenomics of the Human Intestinal Tract (MetaHIT) and others have demonstrated the beneficial functions of the normal gut flora (>35000 species) on health. It is thus G-20 nations in Germany are united for active research on MDR bacteria to stop superbug horror. Interestingly an improved MDR-cure organic phyto-extracts (*Cassia fistula, Suregada multiflora, Syzygium aromaticum and Cinnamomum zeynalicum etc*) inhibits Kolkata superbugs and gives a hope for new drug development as we have characterized active chemicals by MASS, NMR and FT-IR.

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