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Non-Antibiotics: Psychotropic Drugs

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In the 1950s, it was found that many drugs designed for non-infectious diseases can also exhibit antimicrobial properties [1]. These drugs are named as non-antibiotics in pharmacology [2,3]. Figure 1 demonstrates the action of non-antibiotics.

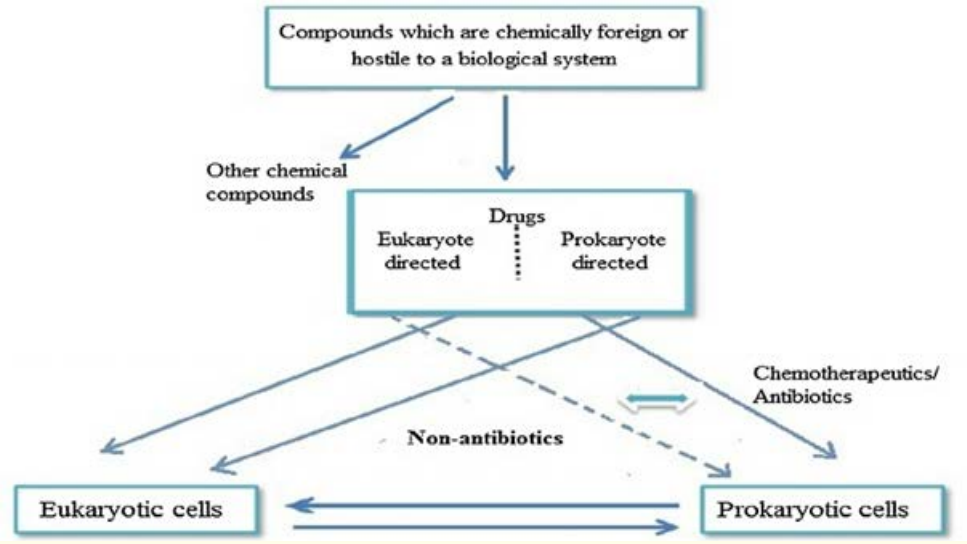

Figure 1: *The concept of non-antibiotics [3].*

The actions of non-antibiotic drugs on microbial growth are different. They can show direct antimicrobial activity by increasing the efficiency of an antibiotic when they are given together (Synergistic effect), or change the pathogenicity of microorganisms or activity on the physiology such as modulating macrophage activity [4].

Among the non-antibiotics, the most studied ones are psychotropic drugs. These psychotropic drugs not only reverse microbial antibiotic resistance but also exhibit direct antimicrobial activity against several biological targets [5].

In 1975, the antimicrobial activity of psychotropic drugs was described. At that time, antibacterial activity of series psychotropic drugs sertraline, paroxetine, fluoxetine and clomipramine was examined against the anaerobic fecal bacteria using agar diffusion and minimum inhibitory concentration (MIC) test. Among them, the phenothiazines and amitriptyline showed antibacterial activity in the MIC's test in the 40 - 640 µg/ml concentration range [6].

Since then, a lot of psychotropic drugs have been examined. The drugs have a significant antimicrobial activity, mainly against Gram-positive bacteria, some against Gram-negative bacteria, Mycobacterium, Yeast and Fungi [5].

Selective serotonin reuptake inhibitors (SSRI) are used widely for the treatment of depression, of chronic pain, menopausal symptoms, and migraine headache prophylaxis [7]. Sertraline is a potent selective serotonin reuptake inhibitors, approved for the treatment of depression, Social phobia, obsessive compulsive, panic and post traumatic disorders [8].

In previous study, sertraline displayed the strongest and widest range of antimicrobial activities against all bacteria, yeast and fungi except *Pseudomonas aeruginosa*. Sertraline but also other psychotropic drugs have been interestingly found to be inactive against *P. aeruginosa* [5].

One scenario to this situation might be that *P. aeruginosa* has protective outer membrane efflux pumps which prevent bacteria from high concentrations of antimicrobial agents accumulation inside the cytoplasm or low outer membrane permeability controlled by the OprD porin production [9].

Interestingly, SSRI group drugs (sertraline, paroxetine, and fluoxetine) and clomipramine exhibited better antibacterial activity against vancomycin resistant enterococci (VRE) compared to parental *Enterococcus faecalis* strain.

In contrast to this observation MRSA(Methicillin-resistant *Staphylococcus aureus*) was more resistant to chemicals tested with respect to parental *Staphylococcus aureus.*

Mycobacterium tuberculosis has been the most sensitive against psychotropic drugs including sertraline, paroxetine, fluoxetine and clomipramine. The drugs were found to display inhibitory effect as low concentration as maximum psychotropic drug serum levels in human metabolism which is close to 2 mg/L.

It is suggested that *in vivo* studies should be conducted to examine potential antimycobacterial activities of the psychotropic drugs alone or in combination with approved tuberculosis drugs [5].

The main limiting factor for the use of non-antibiotic drugs as an antimicrobial agent in mammalian system is that the maximum level in serum remains (approx. 1 mg/L) lower than the concentration required for inhibition of microbial growth [10].

These studies suggest that the use of psychotropic drugs even low concentration, alone or in combination with other antimicrobials can be effective against various type of microorganisms.

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