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Are antibiotics "weapons" against neighbouring bacteria?

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Editorial

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EDITORIAL

The discovery of penicillin opened a new era in the treatment of infectious diseases, known as the "golden age" of antibiotic research. After many decades of antibiotic usage and plenty of lives saved we have assumed that these "magical" chemicals are only synthetized to kill bacteria. However, these metabolites could have a totally different role in the producing microorganisms like, for example, cell communication. This statement is difficult to understand from an anthropogenic point of view. Taking possession of a territory has been always a matter of conflict and, quite frequently, of war. Therefore, we usually believe that microorganisms are constantly fighting against each other in order to occupy the entire environment. And, of course, we assume that one of the best strategies to achieve this propose is producing antibiotics; which are ready to use as weapons against competitors. In this editorial I would like to discuss why several scientists, and myself, think that the main role of antibiotics is different than just killing or combating bacteria. Actually, Professor Emeritus Julian Davies had already opined some time ago that the term "antibiotic" was mainly a pharmaceutical denomination rather than the description of its natural role [1].

There are many reasons for not considering the antibiotics just as weapons in microbial conflicts. Moreover, in my opinion, they could be defined as beneficial molecules for the bacterial community. First of all, there are few evidences that antibiotics are produced by bacteria in the environment or, if so, at sufficient concentrations to produce their presumed weapon effect. All substances (including those producing beneficial effects) can be poisonous when high concentrations are applied. A well-known example is caffeine, which at normal concentrations does not killed humans but when ingested at huge amounts is lethal. The same may occur with antibiotics in bacteria; but scaling the amounts. In fact, several studies have demonstrated that antibiotics, at sub-inhibitory concentrations, exert other effects distinct to killing bacteria like, for example: initiation of developmental changes, acquisition of substrates or promotion of interactions with hosts and biofilm formation [2].

Drug discovery has historically focused on bacteria growing in pure cultures. However, in their natural habitats, microorganisms predominantly live in complex communities called biofilms. The biofilm mode of life provides advantages to these organisms, such as an enhanced resistance towards environmental stresses. This suggests that killing neighbouring bacteria is not the most optimal decision for these organisms. Microbes in a biofilm community gain additional antibiotic resistance which, in some cases, can be a thousand times higher than that corresponding to the single cells [3]. According to this, it makes sense to imagine the antibiotics as signals for cell communication in these complex populations rather than as weapons to kill each other. Actually, it seems that in nature these molecules most likely act together with other metabolites produced by either the same or a distinct bacterium [4].

It is important to note that a huge number of antibiotic-like molecules (normally known as secondary metabolites) are produced by distinct microorganisms. For instance, species belonging to the *Streptomyces* genus have an average of 20 or more secondary metabolite biosynthetic clusters in their genomes [5]. These bacteria normally synthetize one or more compounds with antibiotic activity during their growth as pure cultures in laboratories (conditions in which killing competitors would not be needed).

Many of these compounds have a peak of production and afterwards are degraded or metabolized; pointing to a nutritional function of the antibiotics. Although the selective advantages of antibiotics used as substrates for bacterial growth are yet unclear, it has been clearly shown that many diverse bacteria are able to subsist on several different antibiotics as sole carbon source [6].

Nevertheless, despite the main role of antibiotics in nature was not to kill bacteria these molecules are very useful for humans. The same applies for other bioactive molecules used as anticancer drugs, immunosuppressants or pigments (which their functions are obviously different in the producing strains). Therefore, to conclude, and out of the scope of this journal, I would like to enhance the importance of putting the human efforts into the utilization of the natural resources (including not only living organisms but also materials or energies) for the life benefit rather than for war or destruction.

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