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# Tetracyclines and their Resistance

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## Introduction

Besides the human and veterinary medicine, the antimicrobials have usage in various areas as aquaculture, food technology, agriculture and animal husbandry [1]. The total amount of antimicrobials used worldwide is estimated in 100,000-200,000 tonnes/year [2-4]. Since 1950s, tetracycline (TC) antibiotics which rank second both in the production and usage of antibiotics worldwide have been widely used in human and veterinary medicine to treat bacterial infections and promote animal growth [5-9]. The global sales of TCs were 1.6 billion dollars in 2009 [6-10]. These properties support their usage especially in developing nations [11-13].

TCs, both natural and semisynthetic, form a large group of products produced mainly by Streptomyces spp. They have a broad-spectrum of activities including inhibition of many common Gram-positive and Gram-negative bacteria, chlamydia, rickettsie, etc.; they are distinguished mainly for bacteriostatic action caused by inhibition of protheosynthesis [14-17]. Only a small fraction of TC is absorbed or metabolized in the human body [18,19]. Therefore, they mostly excreted from the body (urine and feces) as unmetabolized parent compound [20]. Active part of TC in urine is approximately 20-55% [21,22]. Human excretion rate for TC in the aquatic environment is high (70%) [6,23]. They have a high aqueous solubility and a long environmental half-life [24,25]. It has been reported that TCs have been found in soils [26], surface water [27,28] and groundwater [22,29].

The residues of antibiotics may cause some adverse effects on organisms and environment. They have chronic toxic effects on terrestrial organisms. They may effect microorganism's resistance [30-32]. Long persistence of antibiotics leads to concern of widespread antibiotic resistant bacteria and resistance genes in the aquatic environment [33]. The antibiotic resistant bacteria

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and genes can no longer be treated with the presently known drugs [9,34,35]. TC resistance of the organisms emerged soon after its discovery six decades ago. In order to impart resistance, microorganisms use various molecular mechanisms (target protection, active efflux, and enzymatic degradation). A deeper understanding of the structure, mechanism, and regulation of the genes and proteins associated with TC resistance will contribute to the development of TC derivatives that overcome resistance [36].

TCs have high risk of occurrence of antibiotic resistant bacteria in various environments. TCs are frequently detected in the surface waters where the effluents of the wastewater treatment plants and agricultural activities reach [37,38]. In order to reduce negative impacts on environment, it is necessary to understand input sources for antibiotics [39].

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