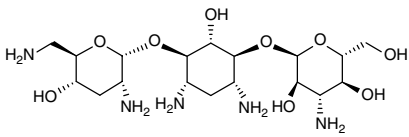
14.5 Aminoglycosides

14.5.1 Streptomycin

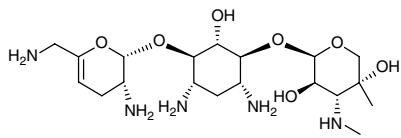
Streptomycin (**4**), the first of the aminoglycosides, was often considered in the West to be the second antibiotic to begin clinical use (during WWII) after penicillin G/V; however, as shown earlier, the use of gramicidin S predated it. It did begin use in wounded soldiers in the late 1944 to early 1945 time frame. Its discovery was formally reported by the Waksman group in 1944 (Schatz et al. 1944) and it was not until 30 years later that its formal synthesis via dihydrostreptomycin was published by Umezawa et al. (1974a, b). The aminoglycosides were used in large quantities and over the years, different variations of the basic structure either were found from nature or were the product of slight chemical modifications to overcome the aminoglycoside-modifying enzymes (AMEs), plasmid-borne enzymes that *N*-acetylate, or *O*-adenylate or *O*-phosphorylate on specific hydroxyl groups in the molecules. Most of the naturally occurring aminoglycosides were discovered between the 1940s and 1970s and classified into three basic groups: streptidine containing (**4**); 2-deoxystreptamine containing (neomycins, paromomycins, kanamycins, gentamicins, tobramycin (**38**), sisomicin, ribostamycins, lividomycins, butirosins, and verdamicin). In addition, there were novel ones other than the two earlier classes, hygromycins, spectinomycin, apramycin, and fortimicins (structures not shown). A very recent paper demonstrated that even 44 years after the introduction of tobramycin in 1974, the compound is still very useful in combatting biofilm-bound *P. aeruginosa* in clinical settings (Müsken et al. 2018).

14.5.2 Plazomicin

The slight modification of sisomicin (**39**), which was originally reported in 1970 from *Micromonospora inyoensis* (Weinstein et al. 1970) that produced the semisynthetic plazomicin (**40**), was described in detail by Galani (2014) with the agent being approved by the US FDA in 2018 for treatment of complex urinary tract infections such as those caused by carbapenem-resistant *Enterobacteriaceae* (CRE) and extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae*.



38; Tobramicin



39; Sisomicin