Nucleoside analogues to combat metronidazole resistant *Trichomonas vaginalis*

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Trichomonas vaginalis is the most common non-viral sexually transmitted organism worldwide, and is associated with vaginitis and birth complications. The 5-nitroimidazole drugs, metronidazole (Mz) and tinidazole, are the only chemotherapeutics available for treating trichomoniasis. However, resistance to these compounds is increasing and alternative chemotherapeutics are needed. Nucleoside analogues (targeting the parasite purine salvage pathway) are likely candidates. Of 33 nucleoside analogues tested, toyocamycin (Ty) and 2-flouro-2-deoxyadenosine (F-dAdo), were highly effective against Mz-susceptible (MzS) *T. vaginalis in vitro* with minimal inhibitory concentrations (MIC) of 3.2 and 1.6 uM, respectively. However, both drugs were less effective against clinically Mz-resistant (MzRC) *T. vaginalis* (MIC of 25 uM). Ty resistance was rapidly induced in these parasites resulting in decreased susceptibility to F-dAdo suggesting cross-resistance between Mz and the nucleoside analogues in MzRC parasites. These data question the suitability of nucleoside analogues as alternative drugs in cases of Mz treatment failure.