ABSTRACT

Vaginal trichomoniasis is a highly prevalent sexually transmitted disease caused by a microaerophilic protozoan *Trichomonas vaginalis*. The disease is one of the most common sexually transmitted disease and can augment the predisposition of individuals to human immunodeficiency virus (HIV) infection. Although the disease can be treated with metronidazole and related 5-nitroimidazole, cases of trichomonal vaginitis which are refractory to standard treatment seems to be increasing. Furthermore, the concerns of mutagenic and carcinogenic potential of metronidazole has been raising. Clearly, new antitrichomonal agents are needed, which more potent against the parasite.

In this study, axenic culture of local strain of *Trichomonas vaginalis* was performed for drugs testing sensitivity. Bisquaternary quinolinium compounds, which belong to the class of AT specific minor groove binding drugs, DNA topoisomerase II inhibitors ellipticine, m-AMSA and fluoroquinolones were investigated for effectiveness against *Trichomonas vaginalis in vitro*, compare to metronidazole as standard drug.

The result showed that *Trichomonas vaginalis* was sensitive to metronidazole under aerobic condition (Minimal Inhibition Concentration, MIC=0.096 μM). Among 14 bisquaternary quinolinium, the most effective compound is an ethyl substitution at R1 and H at R2 and R3, 1-ethyl-4-[4-[4-[4-(1-ethyl-quinolinium)amino]benzamido]anilino]pyridinium salt (SN 7000)(MIC=0.16 μM). Derivatives which have methyl substitution at R1 and amino group at R2 and R3 exert higher MIC than SN 7000. Also derivatives which have functional group substitution at C6, C7 or C8 of quinoline ring show higher MIC than SN 7000. The second low MIC is 0.64 μM and belongs to 1-methyl-4-[4-[4-[4-(1,6-dimethyl-quinolinium)amino]benzamido]anilino]pyridinium salt (SN 8315), 1-methyl-4-[4-[4-[4-(1-methyl-7-chloro-quinolinium)amino]benzamido]anilino]pyridinium salt (SN 8317) and 1-methyl-4-[4-[4-[4-(1-methyl-8-methoxyl-quinolinium)amino]benzamido]anilino]pyridinium salt (SN 8224). The highest MIC

is 128 μM, which belongs to 1-methyl-4-[4-[4-[4-(1-methyl-6-amino-quinolinium)amino]benzamido]anilino]pyridinium salt (SN 13718).

The MIC of ellipticine and m-AMSA are 6.4 μM and 20 μM, respectively. The MIC of ciprofloxacin, ofloxacin and norfloxacin are 64, 960 and 1280 μM, respectively.

Based on these results, ethyl substitution at R1 is very important in relation to effectiveness of bisquaternary quinolinium compounds against *Trichomonas vaginalis*. Next study should pursue the relationship between various substitution at R1 and the activity of the drugs.