proceedings

Abstract

Trichomonacidal Activity of 3,3′-Diindolylmethane (DIM) Is Additive to Metronidazole (MTZ) In Vitro, Supporting Future Oral/Topical Use †

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New, safe, well tolerated, and versatile anti-trichomonal agents for oral and topical use are needed to combat spreading resistance of *Trichomonas vaginalis* to metronidazole (MTZ). Diindolylmethane (DIM) is a non-toxic, cruciferous indole under pharmaceutical development for treatment of cervical and prostatic pre-cancers. Present work reports anti-trichomonal activity of DIM with IC_{50} hundreds of times below the DIM concentration provided in a clinic-ready, sustained-release, vaginal-topical formulation (BR-DIM-VC™ 2%) which has passed vaginal tolerance testing in rabbits. Present in vitro findings against *T. vaginalis* exhibit additive effects of DIM with MTZ, significantly reducing the IC_{50} for MTZ ($p < 0.05$). Combinatorial activity with MTZ was demonstrated using DIM dissolved in DMSO and in a novel self-emulsifying lipid-based formulation, BR-9001, showing a statistically significant enhanced effect of BR-9001 over DIM (DMSO) ($p < 0.05$). Improved bio-delivery of DIM from BR-9001 confirmed DIM's concentration-dependent trichomonacidal activity. Performed in triplicate, the anti-parasitic results are: $IC_{50\ DIM\text{-}DMSO}$ = 91.8 μM, $IC_{50\ BR\text{-}9001}$ = 30.65 μM *, $IC_{50\ MTZ}$ = 2.34 μM, $IC_{50\ MTZ(0.75uM)+DIM(37.5uM)}$ = 1.6 μM * and $IC_{50\ MTZ(0.75uM)+BR9\text{-}001(37.5uM)}$ = 0.8 μM *, * = $p < 0.05$.

Considering the nonexistent therapeutic alternatives for trichomonosis treatment in patients with hypersensitivity to 5-nitroimidazoles or against resistant cases, the combined use of DIM + MTZ for oral and topical administration provides a promising new therapeutic opportunity.

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