البحث الخامس بحث مشترك منشور (غير مستبط من رساله)

فعالية تركيبة الكلوفازيمين والنيتازوكسانيد في علاج داء الكريبتوسبوريديوس المعوي وتعزيز التجدد الخلوي المعوي في الفئران التي تعاني من نقص المناعة

Efficacy of clofazimine and nitazoxanide combination in treating intestinal cryptosporidiosis and enhancing intestinal cellular regeneration in immunocompromised mice

المجلة:

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Abstract:

Cryptosporidium is a widely distributed food and water-borne enteric protozoan that affects a wide range of vertebrates, resulting in life-threatening consequences, particularly in immunocompromised hosts. The lack of effective anti-cryptosporidial drugs may be related to the parasite's unique intestinal location, plus the lack of studies on the process by which the protozoan is able to impair intestinal cellular function. The present work aimed to assess the effect of clofazimine (CFZ), an FDA-approved drug for the treatment of leprosy, as an anti-cryptosporidial drug, using transmission electron microscopy (TEM) and an immunocompromised mouse model. The affected intestinal mucosa with parasitic stages in the infected non-treated group showed signs of severe cellular degeneration, including the loss of tight junctions, deformed and damaged microvilli and irregularly distributed nuclei with a severely vacuolated cytoplasm. Comparatively, nitazoxanide (NTZ) monotherapy showed the lowest efficacy as the drug was associated with the lowest rate of oocyst shedding. In addition, NTZ treatment failed to achieve the return of complete cellular function; abnormalities were evident in the microvilli, cytoplasmic organelles and nuclear features. Clofazimine demonstrated an improvement of the mucosal cellular components, including mitochondria and significantly reduced oocyst shedding. Combined treatment with low-dose CFZ and half-dose NTZ resulted

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in a significant improvement in the enterocyte cellular structures with an absence of intracellular parasitic stages. These results indicate that CFZ, a safe and readily prescribed drug, effectively reduces cryptosporidiosis when used in combination with only half the dose of NTZ. Used in combination, these drugs were shown to be efficient in regaining intestinal cellular activity following Cryptosporidium-induced functional damage in an immunocompromised mouse model.

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