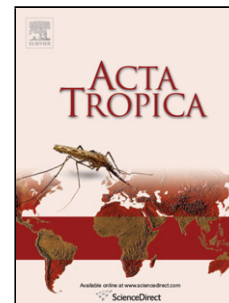


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Authors: Mehdi Farhadi, Ali Haniloo, Kobra Rostamizadeh, Soghrat Faghihzadeh



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Efficiency of flubendazole-loaded mPEG-PCL nanoparticles: A promising formulation against the protoscoleces and cysts of *Echinococcus granulosus*

Mehdi Farhadi¹, Ali Haniilo¹, *, Kobra Rostamizadeh², *, Soghrat Faghilzadeh³

¹ Department of Parasitology and Mycology, School of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran.

² Zanjan Pharmaceutical Nanotechnology Research Center, School of Pharmacy, Zanjan University of Medical Sciences, Zanjan, Iran.

³ Department of Biological statistics and Epidemiology, School of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran

Correspondence should be addressed to:

Ali Haniilo, PhD. (hani@zums.ac.ir)

Kobra Rostamizadeh, MSc., PhD. (rostamizadeh@zums.ac.ir)

Running Title: Flubendazole-loaded mPEG-PCL nanoparticles against protoscoleces and cysts

* Correspondence to: 1) Ali Haniilo, Ph.D., Department of Parasitology and Mycology, School of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran, End of Mahdavi Blvd., Shahrak Karmandan, Zanjan 45139-56111, IRAN.

Phone: +98 (24) 33140243 Fax: +98 (24) 3344 9553. E-mail: hani@zums.ac.ir

* Correspondence to: 2) Kobra Rostamizadeh, MSc., PhD., Zanjan Pharmaceutical Nanotechnology Research Center, School of Pharmacy, Zanjan University of Medical Sciences, Zanjan, Iran, Shahrak Karmandan, Gavazang Road, Zanjan 45139-56184, IRAN.

Phone: +98 (24) 33473635-344. Fax: +98 (24) 33473639. E-mail: rostamizadeh@zums.ac.ir

Abstract

None of the existing drugs can effectively treat the human cystic echinococcosis. This study aimed to improve the efficacy of flubendazole (FLBZ) against the protoscoleces and cysts of *Echinococcus granulosus* by preparing polymeric FLBZ-loaded methoxy polyethylene glycol-polycaprolactone (mPEG-PCL) nanoparticles. The protoscoleces and microcysts were treated with FLBZ-loaded mPEG-PCL nanoparticles (FLBZ-loaded nanoparticles) and free FLBZ at the final concentrations of 1, 5, and 10 µg/mL for 27 and 14 days, respectively. The chemoprophylactic efficacy of the drugs was evaluated in experimentally infected mice. The nanoparticles were stable for 1 month, with an average size of 101.41 ± 5.14 nm and a zeta potential of -19.13 ± 2.56 mV. The drug-loading and entrapment efficiency of the FLBZ-loaded nanoparticles were calculated to be $3.08 \pm 0.15\%$ and $89.16 \pm 2.93\%$, respectively. The incubation of the protoscoleces with the 10-µg/mL nano-formulation for 15 days resulted in 100% mortality, while after incubation with the 10-µg/mL free FLBZ, the viability rate of the protoscoleces was only $44.0\% \pm 5.22\%$. Destruction of the microcysts was observed after 7 days' exposure to the FLBZ-loaded nanoparticles at a concentration of 10 µg/mL. The *in vivo* challenge showed a significant reduction in the weight and number of the cysts ($P < 0.05$) in the mice treated with the FLBZ-loaded nanoparticles, yielding efficacy rates of 94.64% and 70.21%, correspondingly. Transmission electron microscopy revealed extensive ultrastructural damage to the cysts treated with the FLBZ-loaded nanoparticles. The results indicated that the FLBZ-loaded nanoparticles were more effective than the free FLBZ against the protoscoleces and cysts of *E. granulosus* both *in vitro* and *in vivo*.

Keywords: *Echinococcus granulosus*; protoscolex; hydatid cysts; chemoprophylaxis; flubendazole; mPEG-PCL; nanoparticles

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