

Purpose: Combination therapy of Fenofibrate and statins ~~combination therapy~~ is highly recommended by the current clinical guidelines for the treatment of mixed dyslipidemia. In this study, we formulated an innovative delayed-release preparation of fenofibrate ~~was designed to~~ achieve the following: to reduce the risk of muscle toxicity; ~~(caused by simultaneous administration of this combination therapy);~~ by altering the pharmacokinetic profile of fenofibrate; ~~as well as~~ and to improve the oral bioavailability of the modified-release formulation.

Methods: ~~Micronized Fenofibrate~~ was ~~used~~ micronized to prepare drug-loaded cores via a ~~powder powder~~ layering process before performing multiparticulate pellet coating. Different coating formulations were screened, and their in vitro release profiles ~~was/were~~ compared with those of the commercial sustained-release pellets Lipilfen®. Two optimized formulations were evaluated in Beagle dogs ~~using and compared with~~ two reference commercial preparations of fenofibrate (the immediate-release preparation Lipanthyl® and the sustained-release pellets Lipilfen®) ~~as references~~.

Results: The in vivo release of fenofibrate from R1 and R2 selected from in vitro tests exhibited a lag phase, ~~and then~~ followed by rapid and complete drug release. The relative bioavailabilities of R1 and R2 were 100.4% and 201.1%, respectively, which were higher than that of Lipilfen® (67.2%).

Conclusion: ~~The modified fenofibrate pellets developed~~ showed enhanced bioavailability and delayed-release properties; ~~and They have the potential to~~ can potentially improve safety and compliance when co-~~administrated~~ administered with statins. To the best of our knowledge, ~~This is~~ the first report of a delayed-release preparation of fenofibrate ~~preparation~~.

**Comment [A1]:** A compound modifier contains 2 or more words, which act together as one adjective and are connected by hyphens. Hyphens are used with these terms so that their meaning is understood clearly.

**Comment [A2]:** In academic writing, it is important to maintain parallelism in a sentence so that the items being compared can be clearly understood. Here, the sentence has been revised to clearly denote that “in vitro release profiles” are being compared.

**Comment [A3]:** This phrase was revised to maintain consistency with the phrase used previously in the text (under “Purpose”).