Purpose: According to current clinical guidelines, combination therapy of ~~F~~fenofibrate and statins ~~combination therapy~~ is highly recommended ~~by the current clinical guidelines~~ for treating~~treatment of~~ mixed dyslipidemia. In this study, we formulated an innovative delayed-release preparation of fenofibrate ~~was designed~~ 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 f~~Fenofibrate was ~~used~~ micronized and used 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 dog models ~~using~~ and compared with two reference commercial preparations of fenofibrate, Lipanthyl® (the immediate-release preparation) ~~Lipanthyl®~~ and Lipilfen® (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, which was ~~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 m~~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, ~~T~~this is the first report of a delayed-release preparation of fenofibrate ~~preparation~~.

Comment [A1]: The text alongside has been revised to present the intended meaning in a concise manner by retaining only the information that is essential with respect to context.

Comment [A2]: 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 [A3]: 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 [A4]: This phrase was revised to maintain consistency with the phrase used previously in the text (under "Purpose").