
Notice of Retraction

Re: Seely KA, Levi MS, and Prather PL (2009) The dietary polyphenols *trans*-resveratrol and curcumin selectively bind human CB1 cannabinoid receptors with nanomolar affinities and function as antagonists/inverse agonists. *J Pharmacol Exp Ther* 330:31–39 and Highlighted Paper: Polyphenols and Cannabinoid Receptor Functional Agonism *J Pharmacol Exp Ther* 330:1

The article referenced above reported that curcumin and *trans*-resveratrol selectively bind with high nanomolar affinity to the human CB1 cannabinoid receptor (K_i values of 5.9 and 45 nM, respectively) and exert potent pharmacological effects similar to the CB1 receptor inverse agonist rimonabant.

The authors have provided the following explanation:

Subsequent studies in our laboratory and data obtained from three additional independent laboratories (Drs. Jürg Gertsch, Zürich, Switzerland; Roger G. Pertwee, Aberdeen, Scotland, UK, and Vincenzo Di Marzo, Naples, Italy) have failed to replicate these initial findings. Specifically, significant specific binding to either human or mouse CB1 receptors could not be observed below 3 μ M concentrations of *trans*-resveratrol or curcumin. Instead, measurable nonselective CB1/CB2 receptor binding for these polyphenols was similar to the interactions detected with other flavanoid derivatives known to nonspecifically bind to protein surfaces with K_i values $> 10 \mu$ M (Gertsch). Furthermore, unlike the selective CB1 inverse agonist rimonabant (SR141716; hCB1, $K_i < 15$ nM), neither *trans*-resveratrol nor curcumin reversed the constitutive activity of CB1 receptors in Chinese hamster ovary cells at the level of cAMP. We conclude that, although potential weak allosteric effects at the CB1 receptor cannot be excluded, the in vivo data demonstrating antiobesity effects of *trans*-resveratrol and curcumin reported in our initial report may be completely independent of CB1 and CB2 receptor binding interactions. As such, we are retracting our article from publication in the *Journal of Pharmacology and Experimental Therapeutics (JPET)*.

After extensive analysis and review of our original data, regrettably, the exact reason responsible for our initial results, demonstrating high nanomolar affinity binding and function for curcumin and *trans*-resveratrol, is not known. However, we believe that the most likely explanation might result from contamination of our original drug stocks. Specifically, we hypothesize that the common dimethyl sulfoxide stock employed to dissolve all of the polyphenols examined might have been contaminated with the high affinity, selective CB1 antagonist/inverse agonist AM251 that is routinely used in the laboratory.

The authors would like to extend their sincere apology to *JPET* and the scientific community as a whole. It is our hope that the swift correction of our initial report by presentation of findings conducted by four independent laboratories will help to minimize any future ramifications resulting from this very unfortunate situation.

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