Review of: "[Review Article] Pitavastatin: A Comprehensive Overview of its Mechanisms, Pharmacokinetics, Pharmacodynamics, and Adverse Effects"

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Potential competing interests: No potential competing interests to declare.

Title

- To amend. The manuscript's contents discussed broadly on Pitavastatin with unclear correlation between subtopics/sentences, and some information was included without clear indications.

Abstract

- Sound.

Introduction

"The molecule is made up of a dihydroxy heptanoic acid side chain, which binds to the target enzyme, HMG-CoA reductase, just like all statins do."

- Authors could be more precise; change the word 'molecule' to pitavastatin instead.

2. Chemical Structure

Pitavastatin is a widely accepted and efficacious therapy for individuals with combined dyslipidemia as well as hypercholesterolemia, particularly for patients with low HDL-C. That ought to contribute to higher rates of LDL-C target attainment by lowering the risk of undertreatment, minimizing adverse events, and lowering the risk of DDIs in patients who need polypharmacy.

- Suggest to rephrase these sentences for a better flow of information.

Pitavastatin is recognized by its chemical term, (+) monocalcium bis-{(3R,5S,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolyl]-3,5-dihydroxy-6-heptenoate}, and its molecular weight is 880.98.

- Please include the unit for molecular weight.

Figure 1

- Authors did not mention/address Figure 1 anywhere in the text.

3.1 Mechanism of Action

Data from both inside and outside of living organisms; experiments show that statins limit the formation of products from the mevalonate pathway & raise cholesterol accumulation, which impairs the function of β-cells and reduces their sensitivity to insulin and release of it.

- Change to ‘and’.

Compared to other statins, pitavastatin efficiently lowers LDL-C levels at lower dosages.

- Rephrase this sentence.

Figure 2

- Please provide a better-quality image/diagram.

3.2 Other Effects

Pitavastatin has been demonstrated to enhance angiogenesis, decrease the creation of ROS,

- Elaborate this sentence, if possible; how does enhancing angiogenesis lead to decreased ROS production?

Statins have several advantageous benefits that go beyond lowering LDL-C, including reducing inflammation and having positive effects on the endothelium and coagulation cascade.

- The aim of this manuscript is to review pitavastatin. This sentence, including others, has become a general discussion of the ‘statins’ family. Perhaps the authors could rephrase the sentence properly.

4.1 Absorption and Distribution

Pitavastatin's maximum plasma concentration (Cmax) in humans is reached approximately one hour after oral administration; its absolute bioavailability is 51%, and its absorption rate is 80%. The Cmax is decreased when pitavastatin is administered with a high-fat meal, but the AUC (area under the plasma concentration-time curve) remains unaffected.

- These statements have been mentioned in *3. Pharmacodynamics of Pitavastatin*. Please revise the definition of pharmacokinetics and pharmacodynamics.

The passage of PTVS is along basal hepatic cytochrome P450 (CYP) metabolism; as a result, it penetrates the enterohepatic circulation, extending its half-life of elimination (t½) to roughly 11-12 hours.

- What is PTVS?

The primary circulating metabolite is formed when the liver metabolizes it and uridine 5-diphosphate glucuronosyl transferases (UGT1A3 and UGT2B7) glucuronidate it.

- Please rephrase.

5.2 Patients with Diabetes

Asian patients free of severe hypertension or uncontrolled diabetes have been the focus of most pitavastatin research.

- Rephrase.

Against approximately 89% of the studied strains, pitavastatin demonstrated broad-spectrum synergistic interactions with both voriconazole and fluconazole.

- Why is it necessary to include this reference? Omit or elaborate further.

We must determine the best course of action to reduce the hyperglycaemic impact of statins and enhance their cardiovascular benefits.

- Omit ‘we’. Rephrase this sentence.

6. Drug interaction

Polypharmacy, ADRs, and statin-drug interactions: terms such as "statin" (along with others, such as "HMG CoA reductase inhibitor"), terms concerning polypharmacy (such as "polypharmacy" or "interaction" or "concomitant" or "co-morbid"), and words concerning ADRs (such as "adverse drug reaction" or "adverse event" or "side-effect" OR "myopathy" and others were searched).

- There is no flow between this sentence and the previous one.

The literature said that "polypharmacy in old age is the rule rather than the exception."

- Rephrase.

This may be because most physiological processes, such as liver and kidney function, gradually decline with age12.

- Check in-text citation format.

7. Other Side Effects

Elevated levels of cholesterol and triglycerides are linked to a faster decline in kidney function, and dyslipidaemia is more common in chronic kidney disease patients compared to the general population.

- Look for better term/synonyms to replace the word ‘faster’.

It has been demonstrated that the statin drug class is a novel class of medications with pharmacological advantages in a variety of solid tumours.

- Previous sentence mentioned about prevalence of CKD and complication of CKD; how does the authors relate with sudden statement on solid tumours?

Pitavastatin, the only lipid-lowering research with statins, has shown a correlation between drug-induced increases in HDL-C and decreased cardiovascular risk.

- What does it mean with ‘the only lipid-lowering research with statins’?

Pitavastatin causes apoptosis. It shows that using two extracts, PTVS exposes the cell feasibility: sunflower oil, which dramatically restored the action of PTVS in cell proliferation, and milk, which cannot verify that the results in the assay reflected cell death.

- What does it mean with ‘and milk, which cannot verify that the results in the assay reflected cell death’?

Few studies suggest that using statins causes skeletal muscle contractions to behave favourably.

- Please rephrase.

8. Discussions

HMG coenzyme hydroxymethyl One of the drugs that doctors prescribe most frequently in Asia is a reductase (HMGCoA) inhibitor, sometimes known as a statin.

- Change the word ‘one’ to numeral form.

The primary outcome of this investigation was the considerable reduction of cardiovascular events in individuals with lipid disorders who had more than one hazard component for ASCVD when PTVS (2 mg/day) medication was administered.

- Is this the correct way to write dosage?

References

- Please check the format.

General comments

1. Suggest for proofreading; major concern on grammatical errors, punctuation, abbreviation, etc.
2. Major amendments/rephrasing of sentences to aid readers and to have a better flow of information from one to another.
3. The manuscript broadly discusses the topic of Pitavastatin but is not clearly focused on Pitavastatin.
4. Some sentences were repeated numerous times.
5. Every piece of information on Pitavastatin was included in the manuscript without considering/elaborating on the necessity of such sentences.
6. There is too much repetition of information.