Interaction CBD/HydroxyChloroquine :

It seems the main metabolic route for chloroquine is via N-de-ethylation. There are two ethyl groups on the tertiary nitrogen which can be removed sequentially. It seems the main enzymes responsible for this reaction are CYP3A4 and CYP2C8, with a small contribution from CYP2D6 (Projean et al 2003, DMD 31(6) 748-754). Although CBD inhibits all 3 of these CYPs in vitro, it is very weak on CYP2D6 and has been shown in a human DDI study not to affect CYP3A4 activity. We cannot rule out a potential effect of CBD to inhibit clearance of chloroquine via CYP2C8 inhibition. We do see a clinically relevant effect of CBD on N-CLB clearance through inhibition of a closely related CYP (CYP2C19). However, as CYP3A4 metabolism is not affected, the overall effect on chloroquine may not be large (for N-CLB there is very little metabolism other than via CYP2C19 and so it is a very sensitive substrate).

There is no reason to expect an effect of chloroquine on exposure to CBD (chloroquine may inhibit CYP2D6 metabolism but this is not relevant for CBD clearance).

Interactions Stiripentol/Chloroquine :

Cytochrome P450 2C8 and CYP3A4/5 are involved in chloroquine metabolism in human liver microsomes.

At therapeutic concentrations Stiripentol significantly inhibits several CYP450 iso-enzymes, notably 3A4 and 2C8 (DIACOMIT Prescribing Information https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/206709s000,207223s000lbl.pdf ). Consequently, PK interactions with chloroquine can be expected. Such interaction could lead to an increase in systemic concentrations of chloroquine and of its side effects, particularly cardiac.

Biocodex position is that the association of Stiripentol and Chloroquine should preferably be avoided.