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Selective Mefloquine (MFQ) enantiomeric derivatives as potent anti-cancer agents

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Several studies have been carried out demonstrating the anti-cancer (anti-metastatic) effects of Mefloquine on cancer cells. Its mechanism of action is provided by its mimicking the green structure pictured in Figure 1 (named PDF), that plays a role in carcinogenic adhesion. By mimicking a cancer stem cell's structure, mefloquine may have an ability to inhibit cancer cells adhesions and disintegrate tumors, making them available to the attack of white blood cells (Leukocytes).

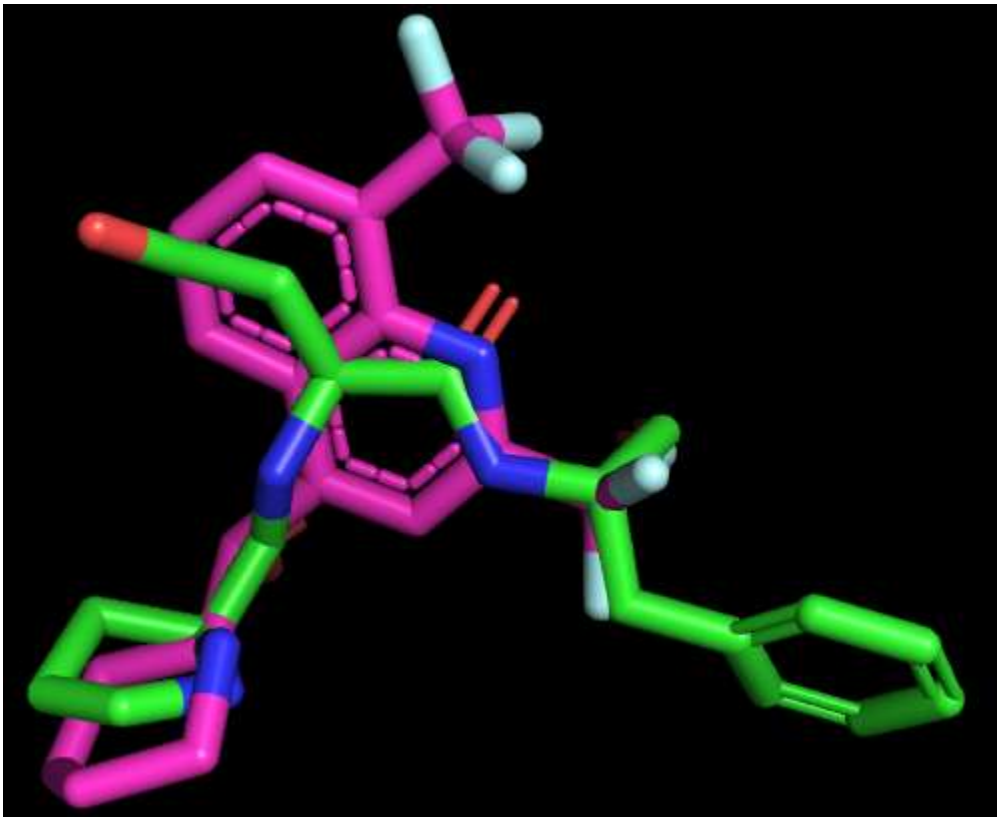


Figure 1. PDF (green) vs MFQ (fuchsia)

Nonetheless, figure 2 shows how an enantiomer could be a more potent candidate as it would be far more misleading than the originating enantiomer, currently in the market. Side effects from the compound are due to the lack of selectivity, and are primarily gastrointestinal and neurotoxic. The psychiatric and neurological adverse-reactions are due to mefloquine's ability to interacting with the alpha subunit isoform of human Guanine nucleotide-binding protein (Gnas-2) and the promethazine-like structure, may make it likely to being absorbed at Central Nervous System (CNS) level, producing neurotoxicity. It is thus why I propose the following derivatives as novel potent anti-cancer agents, likely curative, and that shouldn't provoke as many side effects as the originator MFQ ligand.

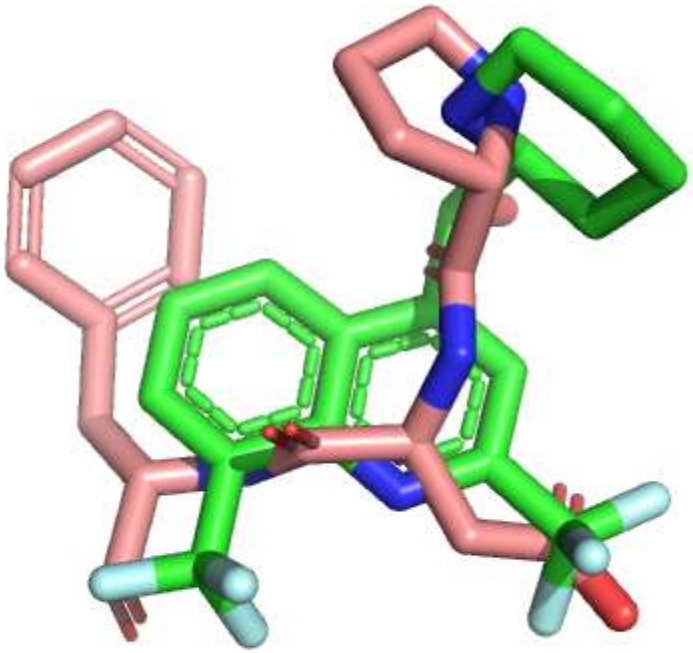
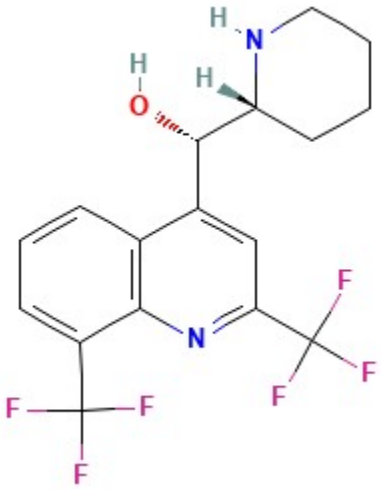


Figure 2. The mefloquine enantiomer, looks like a better mimicker of the PDF. The racemates are already produced by Swiss drug company Hoffmann-La Roche and are both currently on the market.

New derivative drugs are hereby proposed to replace the originator compound, mefloquine (MFQ), whose side effects are pretty demarcated, particularly due to the piperidine ring structure, that makes it neurotoxic, as well as its difficult metabolism making its hepatic metabolism specifically harsh. Although the CF_3 substitute is favored for its renal protective activity and for kidney clearance, it is thereby substituted with a carbon-rich isoster to enhance hydrophobicity.



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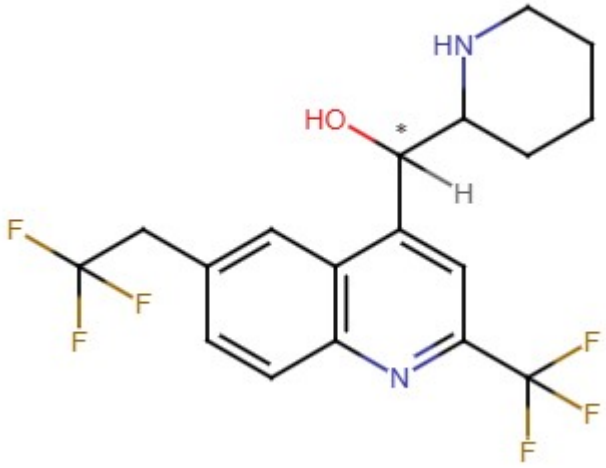

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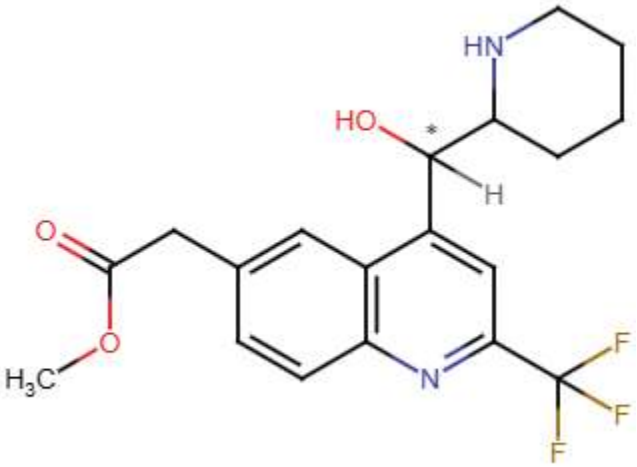

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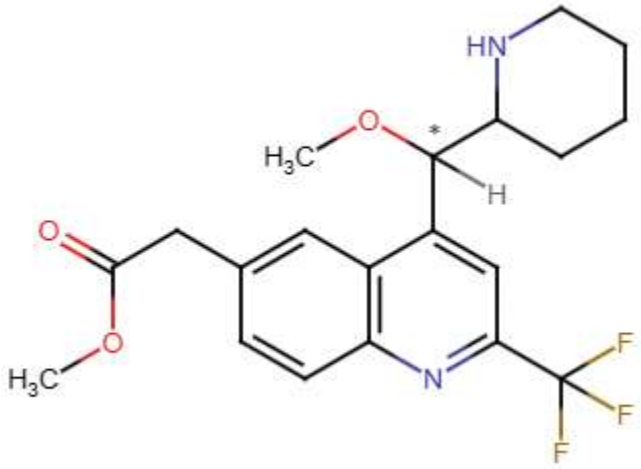

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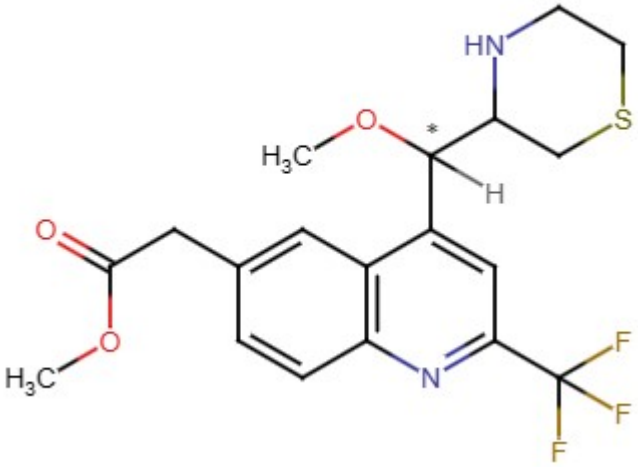

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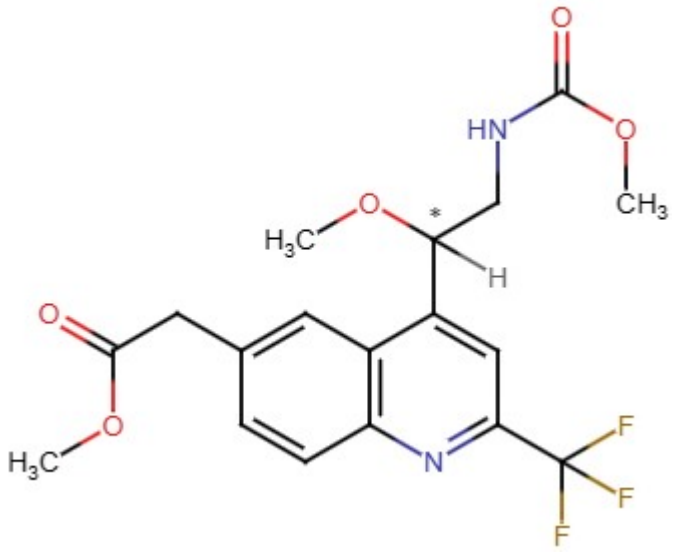

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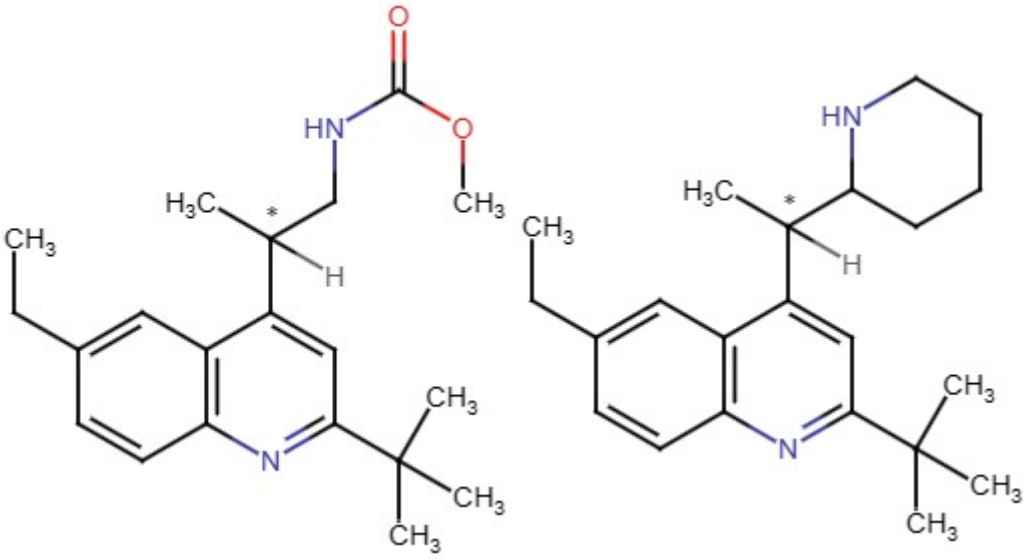

g h

Figure 3. Drug development from mefloquine (compound *a*) to its derivative enantiomers. Their structures might lead to higher potency and in the cases of compounds *e-h*, to higher selectivity, hydrophobicity, reducing absorption at CNS level. These are preliminary designs for the purposes of *in vitro* or toxicology studies.

This short column is an attempt to designing potent and selective mefloquine-like derivatives for the purposes of *in vitro* studies, in the treatment and prevention of

metastatic cancers, to mitigate adverse side events, typical of the chemotherapeutic anti-parasitic agent, post-administration.

No conflicts of interest to disclose.