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The existing armamentarium of drugs for the treatment and prevention of malaria is limited primarily by the resistance and cross resistance between closely related drugs. Therefore, today antimalarial development pipeline is focusing not only on development of new compounds with novel mechanism of action which are long and risky but also on developing drug combinations that have independent modes of action. Combination therapy (CT) can be used to enhance drug efficacy and prevent resistance and is defined as the simultaneous use of two or more blood schizontocidal drugs with independent mechanism of action and different biochemical targets in the parasite giving synergistic or additive effects. WHO recommends that artemisinin based combinations therapies should be preferred for malaria caused by Plasmodium falciparum. However, the major challenges existing in the deployment and use of antimalarial drug combination therapies are operational obstacles to implementation especially compliance. Now with the increased use of new combinations, monitoring of potential drug interactions is urgently required. Although there are reports on synergism or additive potential of two or more antimalarial drugs in a therapy, there are no published reports on the interaction between two of the active principles. Moreover, not much information is revealed about their compatibility with each other in triple regimen.

The compatibility of drugs in a combined preparation or combined therapy is critical factor for the development of pharmaceutical formulations. So, it is envisaged to predict any specific and non-specific interaction between the drugs prescribed in double and triple regimen therapy in combined dosage forms using various techniques such as DSC, PXRD, FTIR, MRC and solution calorimetry.

Artemisinin and its derivatives have been reported to exhibit poor water solubility and bioavailability. Solubility is one of the important parameter to achieve desired concentration of drug in systemic circulation for pharmacological response to be shown. The solubility/dissolution behavior of a drug is key determinant to its oral bioavailability, which leads to effect the therapeutic index of these antimalarial drugs. Out of various strategies developed by biopharmaceutical scientist to enhance the solubility and dissolution of these poorly water soluble drugs is to prepare alternative crystal forms with improved physicochemical parameters. Various solid forms of the active drug having different morphology and crystal habit which is an important variable for the pharmaceutical manufacturing. Whereas, differences in solubility of
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the different forms have implications on the absorption of the active drug from its dosage form \textsuperscript{233}, by affecting their dissolution rate and possibly the mass transport of the molecules. However, the extensive screening utilizing various solvents as prescribed by ICH guidelines is lacking. Therefore, it is envisaged to prepare the different crystal forms with improved physicochemical properties of these antimalarial drugs. The various crystal forms are characterized and subjected to solubility and dissolution studies to select the appropriate form with improved physicochemical parameters. Literature survey has revealed that only few studies are reported about the existence of various crystal forms/polymorphs.\textsuperscript{234-235}

These antimalarial drugs are not only exhibit poor water solubility and bioavailability, but also have stability problem and degrades in acidic conditions and associated risk of toxicity. Therefore, it is planned to encage these drug molecules into the CD cavity. CDs are oligosaccharides molecules which are used to improve the aqueous solubility and dissolution rate, stability, decrease volatility, alter release rates, modify local irritation, and bioavailability of lipophilic drugs via complex formation and has been widely practiced in the field of pharmaceutical formulation. The rational design of formulation which takes advantage of cyclodextrin inclusion complexation requires a good understanding of encapsulation equilibrium through parameters such as stoichiometry and binding constant of the inclusion complex. The emphasis is laid on to determine the stability constant, enthalpy of binding and entropy of binding associated with the complexation. The inclusion modes suggested by the NMR are further supported by Docking studies utilizing Fast Rigid Exhaustive Docking acronym. The pharmacological activity of complexed drugs are performed and correlated with the complexing abilities of different CDs.

Antimalarials are extensively used class of drugs and many studies are reported in literature about the existence of cyclodextrin complexes of these antimalarial drugs. Three reports demonstrated the effect of HP-\(\beta\)-CD and \(\alpha\)-CD on the solubility of pyrimethamine.\textsuperscript{236-238} However, thermodynamic parameters accompanying the encapsulation as well as \textit{in vivo} studies are completely lacking. Regarding the CD complexes of artemether, arteether and artesunate,\textsuperscript{239-240} no detailed characterization, thermodynamic parameters as well as \textit{in vivo} studies are available except one report on artemether\textsuperscript{241} where, the authors have used only HP-\(\beta\)-CD in their studies. Moreover, no attempt was made to compare the complexing abilities of other suitable derivatives of \(\beta\)-CD with native \(\beta\)-CD.