Multidrug resistant parasites are the biggest therapeutic challenge to health care in most malaria-endemic areas. The rising problem of morbidity and mortality justify the search and adoption of new tools and measures to minimize the impact of malaria. Homeopathy is the second largest system in the world that uses small doses of various natural substances to stimulate autoregulatory and self-healing process. Homeopathic drugs are economical and have been claimed for their efficacy without inflicting side effects but, it lacks some evidence based research and data in order to prove its efficacy with acceptable scientific norms. The present study has been undertaken to explore what homeopathic treatment could offer, both in monotherapy and combination therapy for cure as well as prophylaxis. An alternate method of treatment using artesunate based combination with homeopathic medicine has been also evaluated against lethal rodent malaria parasite.

In this study, the anti-plasmodial efficacy of homeopathic mother tinctures (ϕ) of *Cinchona officinalis* (Chin.), *Chelidonium majus* (Chel.) and *Arsenicum album* (Ars.) and their various potencies (6C, 30C and 200C) have been evaluated against chloroquine sensitive strain of *Plasmodium berghei* (NK-65) in murine mouse model. The cultivation of *Plasmodium* species *in vitro* has been a major research success, which has paved the way for the understanding of parasite and rapid screening of antimalarial drugs for their effectiveness. A preliminary *in vitro* antimalarial screening of mother tincture and all the different potencies of Chin., Chel. and Ars. was undertaken. The study pointed towards the presence of significant antiplasmodial efficacy in these with maximum schizont maturation inhibition of 80% in Chin. ϕ, Chin. 30 and Chel. 30. The positive control chloroquine (10µM) exhibited 95.4±1.6% schizont maturation inhibition *in vitro*.

*In vivo* studies were undertaken out to evaluate suppressive, preventive and curative efficacy of homeopathic medicines in *P. berghei* infected BALB/c mice. Homeopathic preparations of Chin. 30, Chel. 30 and Ars. 30 showed significant (p<0.0005) parasite inhibition with considerably enhanced mean survival time (MST). Maximum chemosuppression was observed by Chin. 30 (100%) followed by Chin. ϕ (94%), Chel. 30 (85.3%) and Ars. 30 (85.3%). The combination of Chin. 30+Chel. 30 also exhibited 100% chemosuppression by the 28th day of follow up period. Artesunate based combination therapy with Chin. ϕ and Chin. 30 potency also showed extremely statistically significant (p<0.0005) antiplasmodial efficacy with complete parasite clearance after day 7. Chin. 30 and combination of Chin. 30+Chel. 30 showed 97.9% and 89.2% preventive activity respectively which was more than the standard drug pyrimethamine (83.8%). Combination of AS+Chin. ϕ
and AS+Chin. 30 exhibited significant preventive (93%) and curative activities (91.9% and 92.6%) respectively on day 7 with enhanced MST of mice in these groups.

Liver and kidney of host are affected in the early stage of malaria leading to significant alterations in the physiology and morphology of these tissues leading to hepatic dysfunction and acute renal failure. Therefore, the functional organization of liver and kidney after the homeopathic treatment has also been evaluated by monitoring the changes in levels of marker enzymes along with histopathological changes of liver and kidney of treated mice. Present study confirms that monotherapy of Chin. 30 and combination therapy of Chin. 30+Chel. 30, AS+Chin. ϕ and AS+Chin. 30 decreased the hepatic (ALP, bilirubin, SGOT and SGPT) and renal (Creatinine, urea, uric acid and BUN) indices in comparison to the infected control. The safety of the above drugs was further confirmed by normal architecture of liver and kidney as observed in histological studies. Whereas, the positive controls CQ(5mg/kg) and AS(4mg/kg)+SP(1.2mg/kg) treated groups exhibited higher levels of bilirubin concentration. Histological studies also exhibited disturbed structural integrity of liver and kidney. It points towards the better therapeutic efficacy of homeopathic drugs in comparison to the standard drug/drug combination.

Present study confirms the better safety and antimalarial efficacy of homeopathic medicine and their combinations. This study gives an insight about the use of alternate system of medicine for the treatment of malaria, which will be effective in terms of cost and antimalarial efficacy without any drug pressure for resistance and side effects. These findings also demonstrate that the combination of two different homeopathic drugs is also effective. The combination of homeopathy with standard allopathic drug artemunate has also been proved to be very effective in combating lethal murine malaria and showed better therapeutic efficacy in comparison to other drug regimens.