



ANTIMALARIAL ACTIVITIES OF COLOROTANE SESQUITERPENES ISOLATED FROM WARBURGIA UGANDENSIS: DOCKING AND MEDICINAL ANALYSIS



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1-ABSTRACT
The observation of therapeutic failures of multiple antimalarial protocols in sub-Saharan areas where acute malnutrition is highly prevalent is the main motivation for the choice of this topic. In view of the geographically isolated failures of artemisinin-based combination therapies, the problem of standardising protocols to assess the clinical relationship between malaria and malnutrition requires imperative reflection. To this end, the ethnobotanically validated inhibition of acute malaria (more so than chloroquine) by daily intake of *Warburgia ugandensis* tea by Ugandan and Kenyan populations needs to be exploited. The geometric data B3PW91/6-31+G(d,p) is used as a starting point for each sesquiterpene colorotane. The evaluation of antimalarial activity was implemented by studying the ligand-analysis interaction of the plasmepsin X protein. The pharmacokinetic profile by applying Lipinski's, Oprea's and Verdonk's constraints was done.

2-MOLECULAR LIBRARY

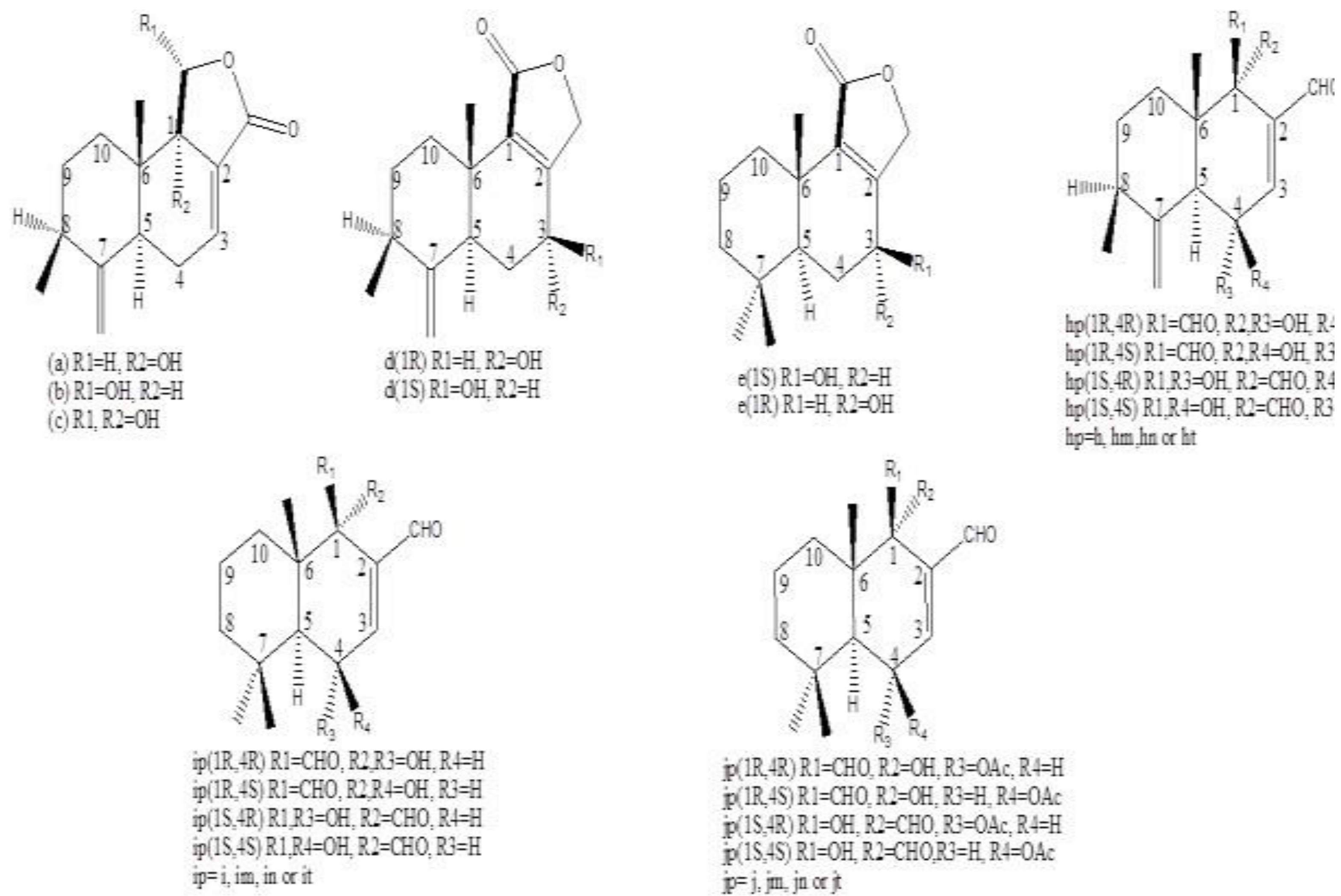


Figure 1: numbering system adopted for the molecular library focused colorotane sesquiterpenes

3-RESULTS

The affinity of the ligand-plasmepsin X protein bond of our molecules are ranging from -7.13 to 4.81 kcal/mol. On the basis of this criterion, (5aS,7S,9aS,9bS)-1,5a,6,7,8,9,9a,9b-octahydro-1-hydroxy-7,9a-dimethyl-6-methylenenaphtho[2,1-c]furan-3(5H)-one structure **(b)** can be elected as a structure with high affinity to the plasmepsin X protein. The examination of the potassium ion channel of the HERG can block the contribution to the electrical activity of the heart.

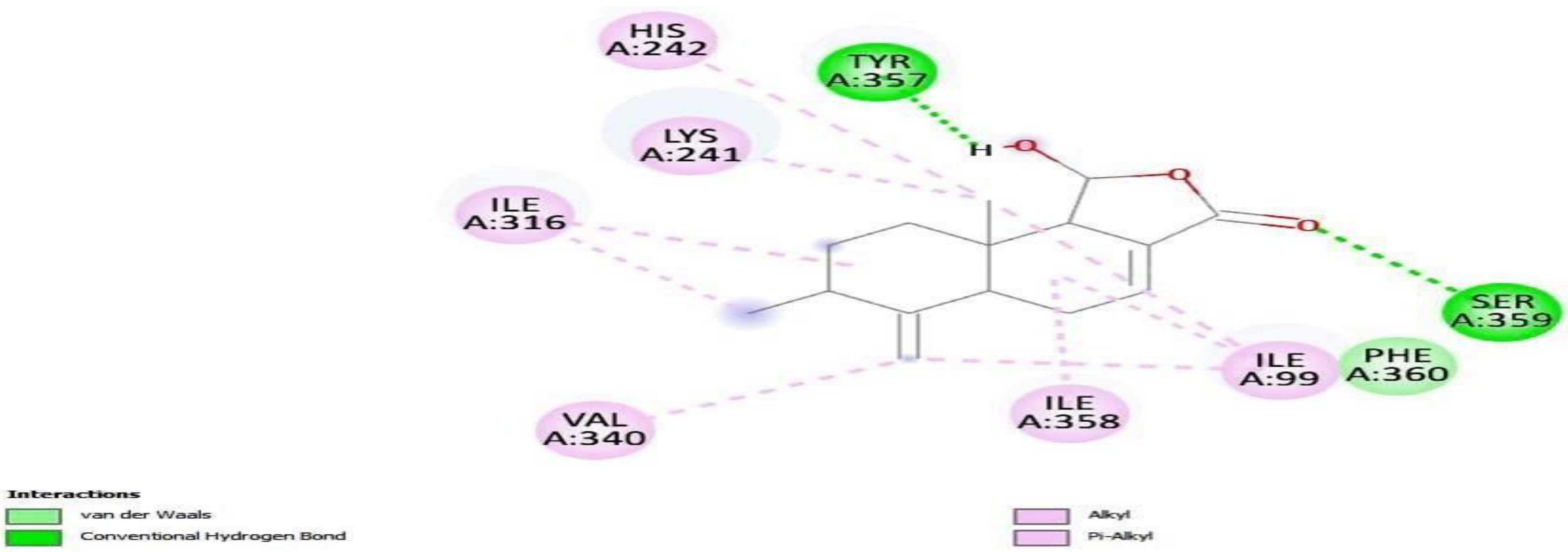


Figure 2: 2D interaction diagram of b compound and plasmepsin X protein target

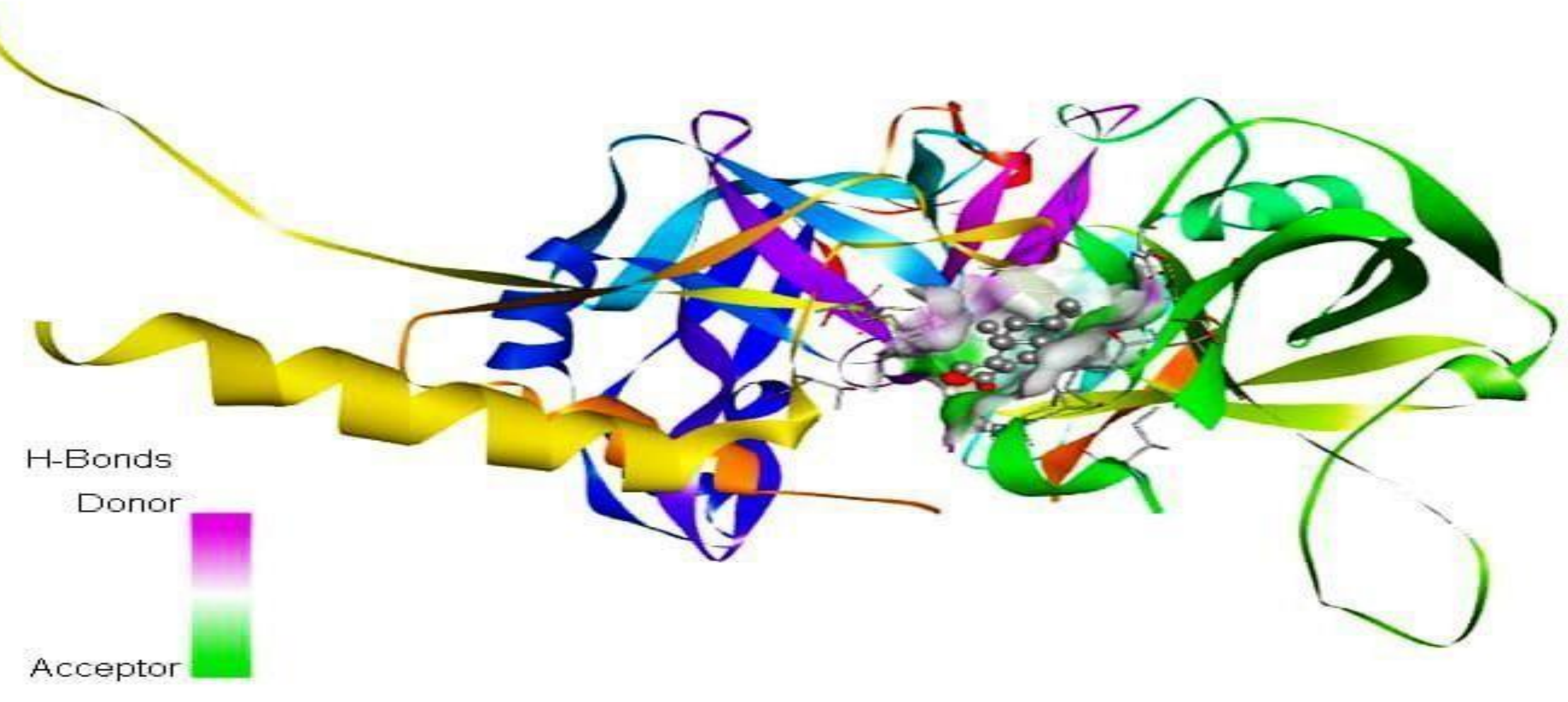


Figure 3: 3D representation of molecular electrostatic potential interaction between b compound and plasmepsin X protein target.

4-CONCLUSION

This work is focused on investigation of molecules that can block simultaneously malaria and malnutrition in order to standardize protocols (to assess the clinical relationship between malaria and malnutrition). Our results shows that our structure b can be elected as a best antimalarial in the molecular library but will not be able to cross skin membrane, gastrointestinal membrane, and will be able to carry the blood-brain membrane. It can be transported by human serum albumin but presage cardiac toxicity.

5-ACKNOWLEDGEMENTS

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