



Molecular Docking of Bufadienolides in *Bryophyllum pinnatum* as Potential Alternatives to Digoxin: inhibiting the Na/K ATPase Pump in cardiac cells for Heart Failure

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ABSTRACT

Heart failure is a condition characterized by the heart's inability to pump enough blood to meet the body's needs, resulting in symptoms such as fatigue, shortness of breath, and fluid retention. Digoxin, a commonly prescribed medication for heart failure, improves heart function by inhibiting the Na/K ATPase pump in cardiac cells, leading to increased intracellular calcium levels and enhanced myocardial contractility. However, the narrow therapeutic index of digoxin poses a significant challenge, necessitating careful monitoring of blood levels to prevent toxicity. Moreover, digoxin's potential drug interactions can result in adverse effects and reduced effectiveness. As an alternative, bufadienolides derived from plants like *Bryophyllum pinnatum* have emerged as promising cardiac glycosides. In a comparative study using molecular docking and pharmacokinetic profiling, bufadienolides demonstrated favourable binding interactions with the sodium-potassium ATPase pump, similar to digoxin. Furthermore, pharmacokinetic profiling indicated a wider therapeutic index for bufadienolides, suggesting a lower risk of toxicity compared to digoxin. These findings highlight the potential of bufadienolides as alternative treatments for heart failure.

Keywords: Bufadienolides, *Bryophyllum pinnatum*, cardiac glycosides, molecular docking, ATPase pump

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INTRODUCTION

- Heart failure is a chronic and progressive condition characterized by the inability of the heart to pump sufficient blood to meet the body's needs .
- It is a global health problem with significant morbidity, mortality, and economic burden.
- Digoxin, a cardiac glycoside, has been used for decades in the treatment of heart failure. However, its use has declined over the years due to concerns about its narrow therapeutic index, the potential for toxicity,
- As an alternative, bufadienolides derived from *Bryophyllum pinnatum* plants have emerged as promising cardiac glycosides because of wider therapeutic index.

METHODOLOGY

- Phytochemicals were obtained from Pubchem, geometry optimisation was done on the structures of the phytochemicals to obtain the most stable conformation
- Na/K ATPase pump was obtained from the RCSB Protein Data Bank (PDB). The protein structure was prepared for molecular docking.
- Molecular docking software (PyRx), visualiser (PyMol, Biovia Discovery Studio), were used to obtain the binding affinity, which was used to calculate the inhibition constant (k_i).
- Other pharmacokinetic parameters obtained were analysed using webserver (ADMETSar2, Molinspiration and SwissADME).

Figure 1. Bryophyllum leaf



Figure 2. 7DDH



Figure 3. Digoxin.

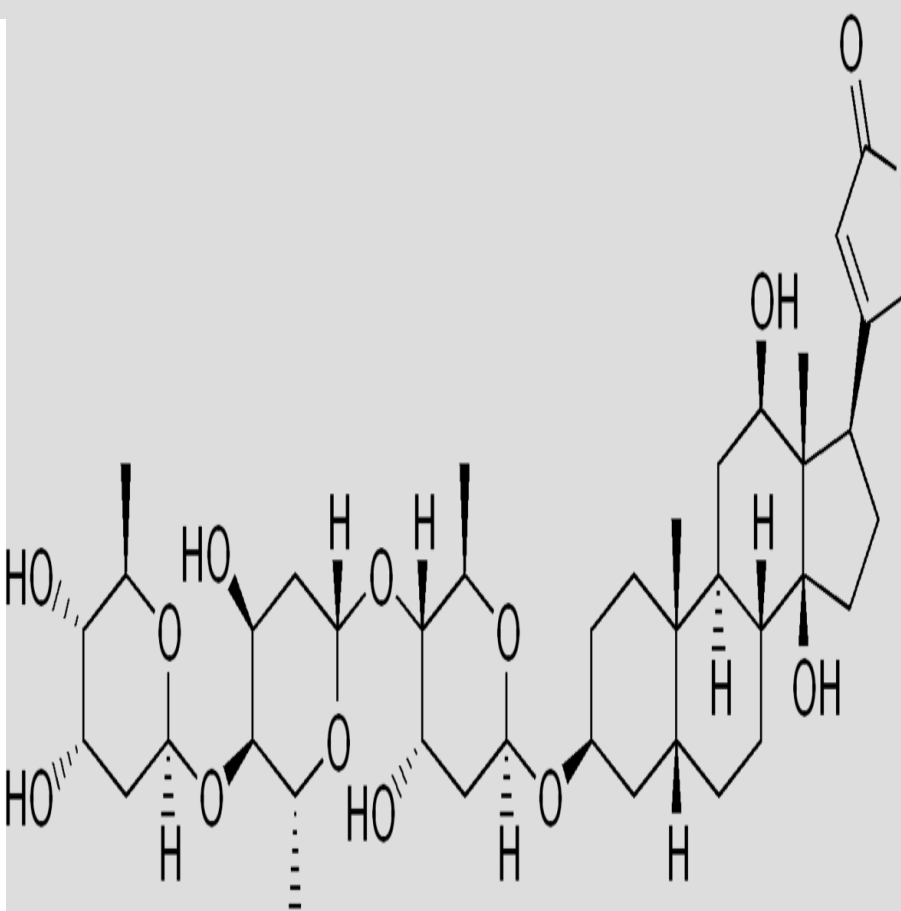
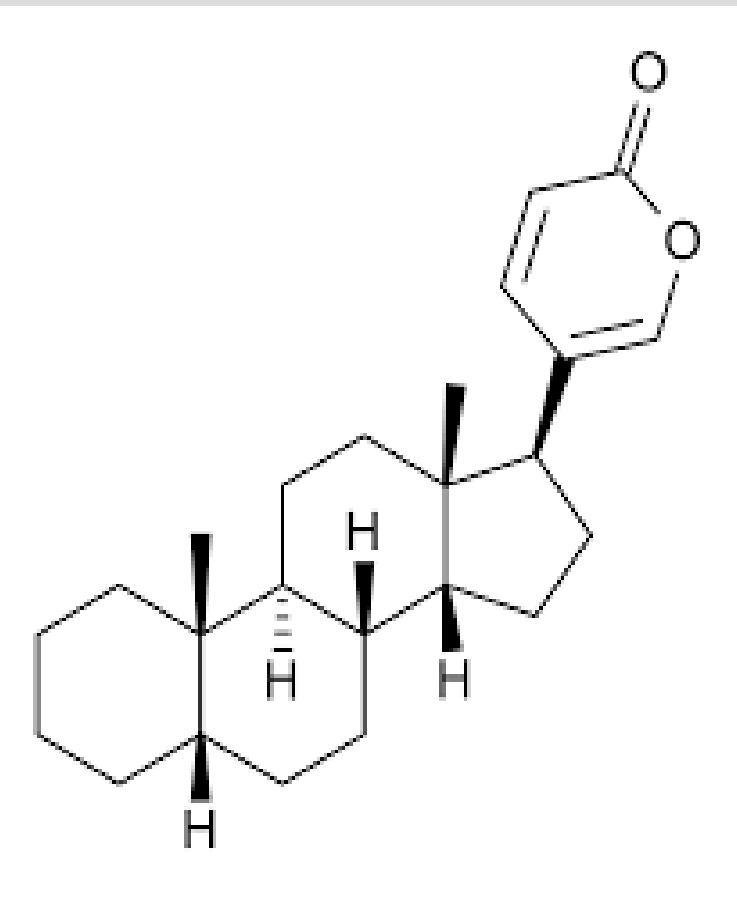


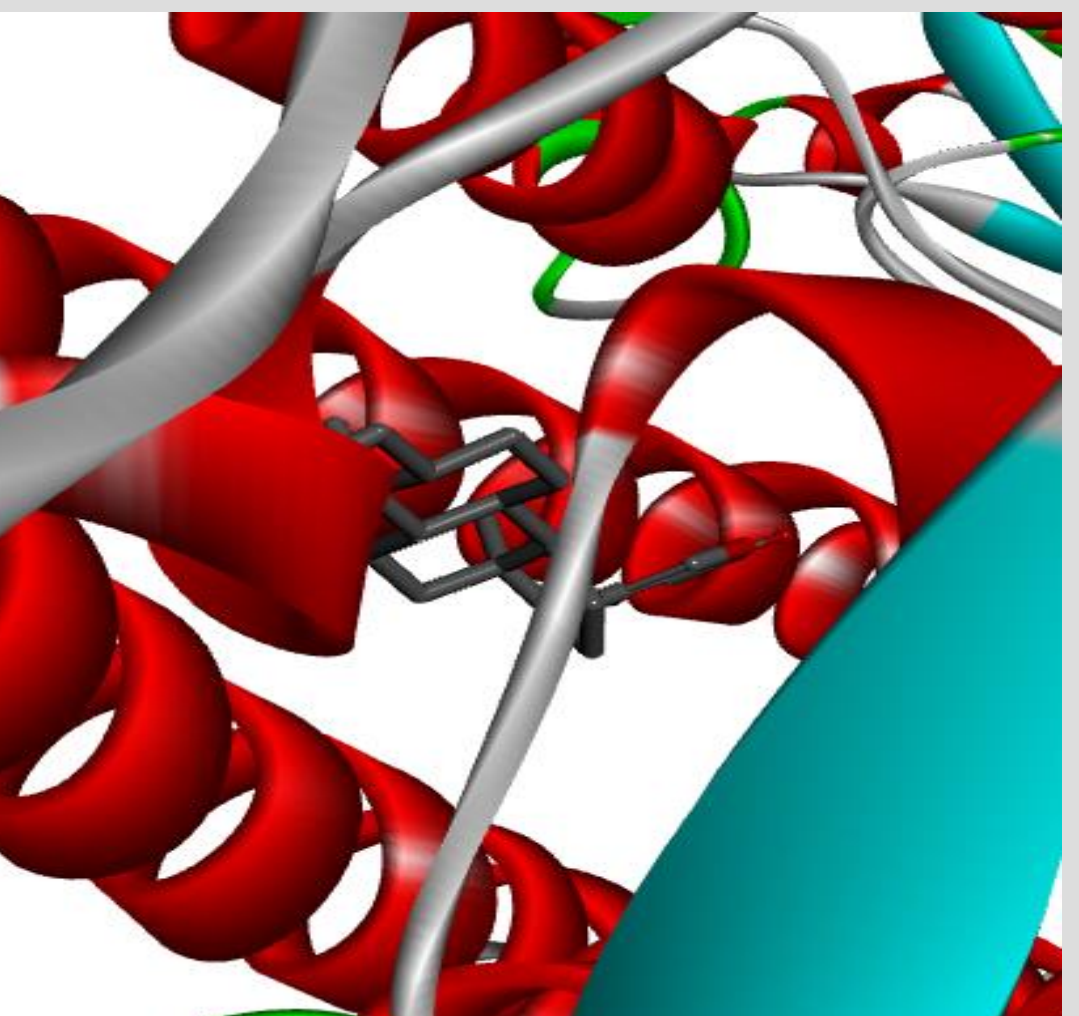
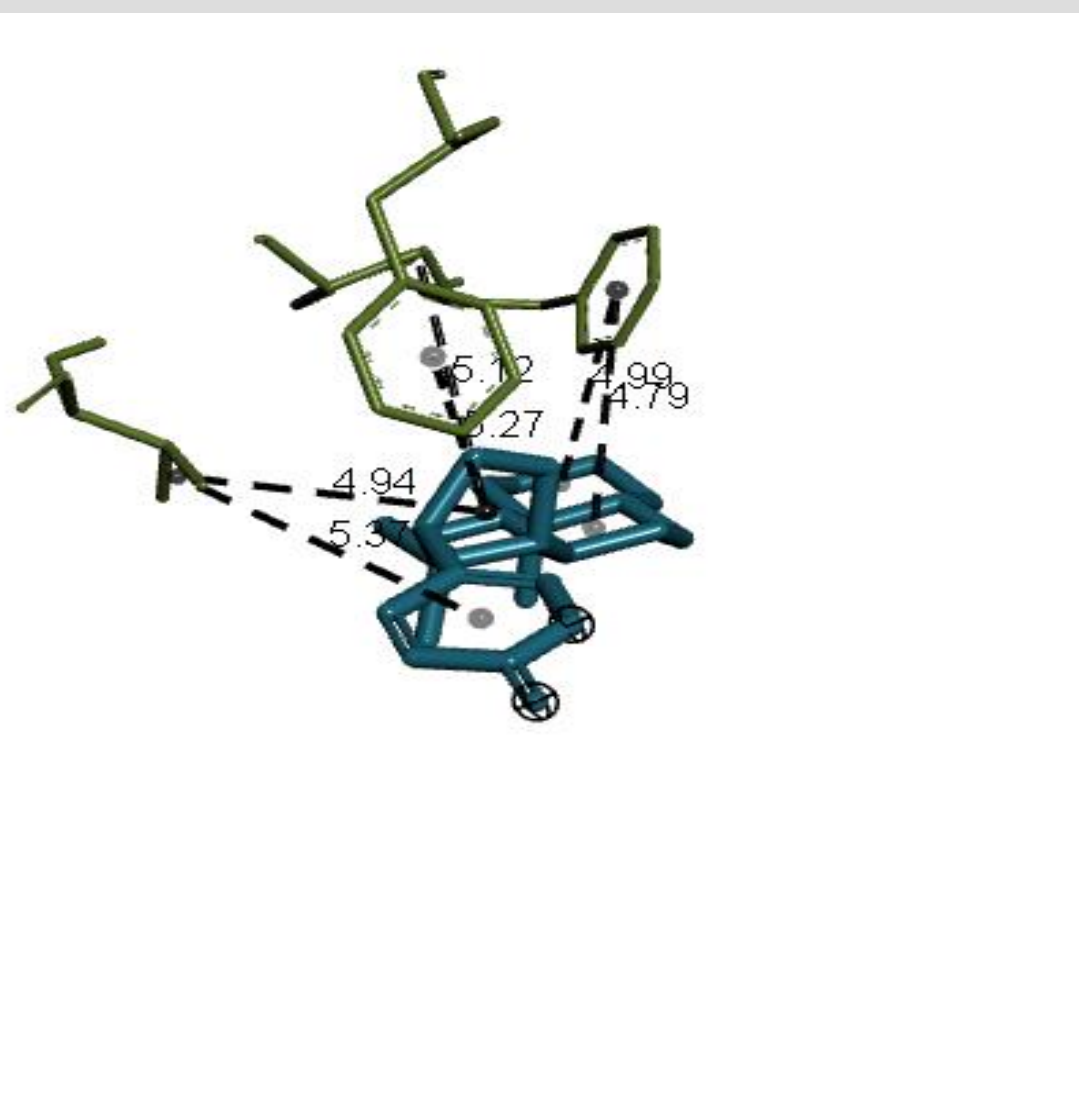
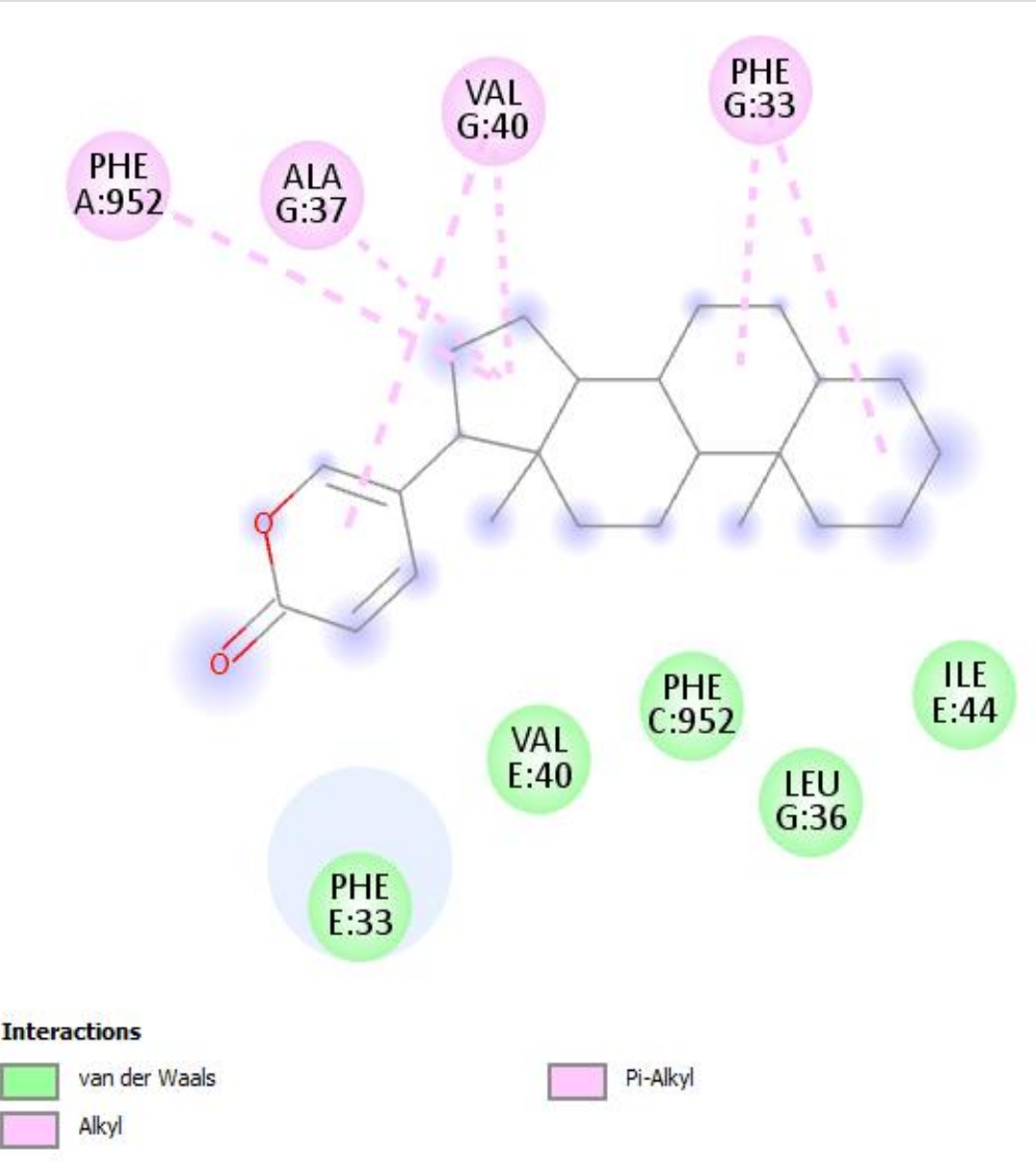
Figure 4. Bufadienolide.



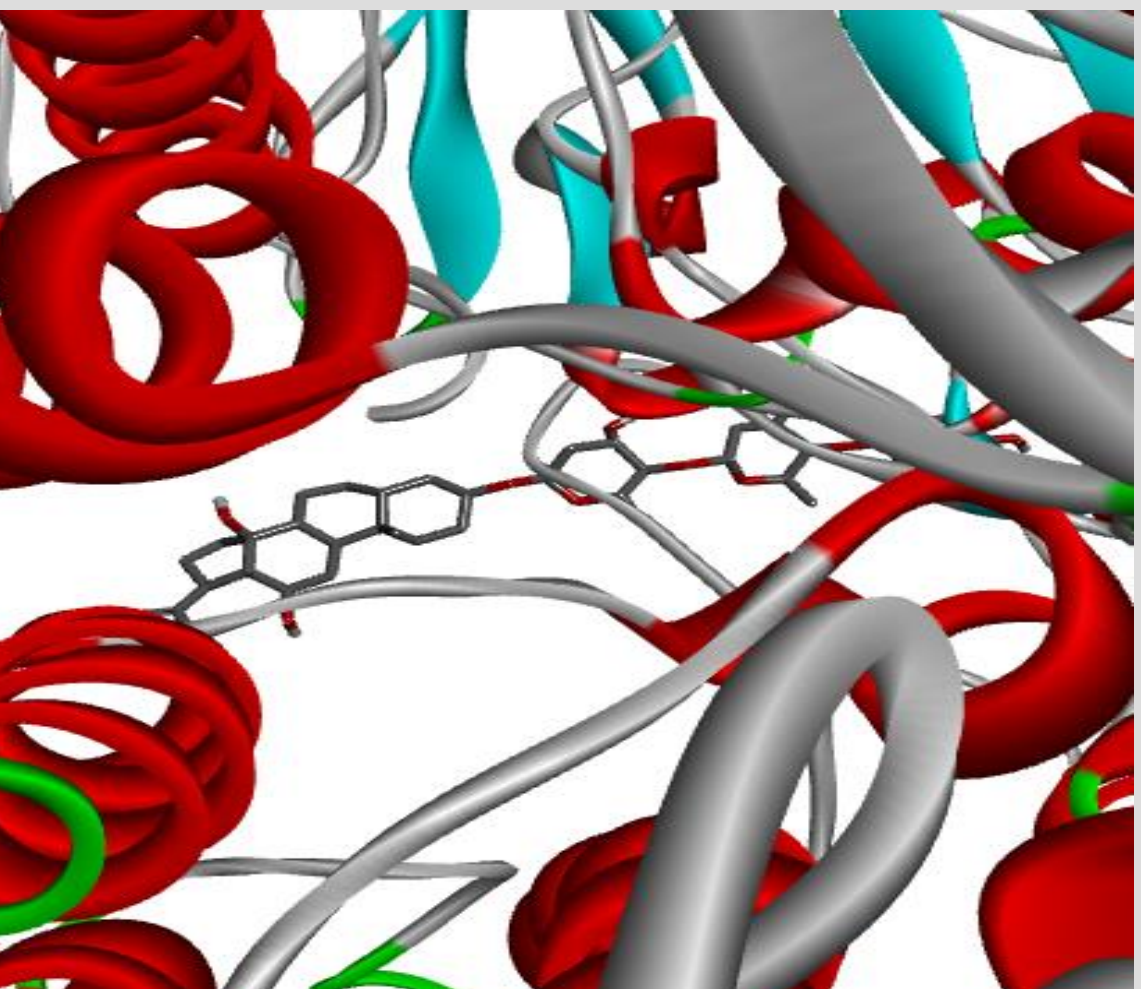
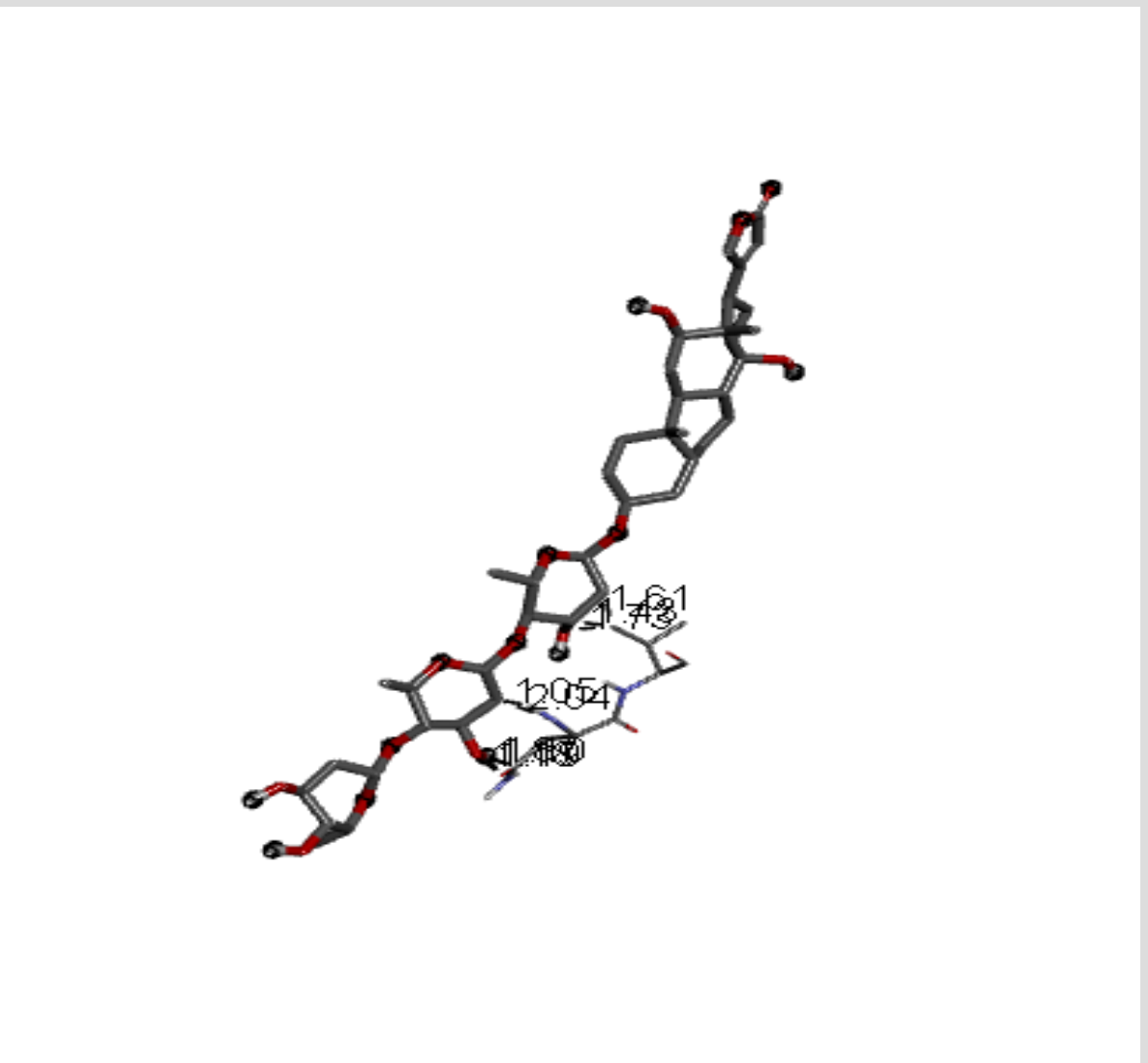
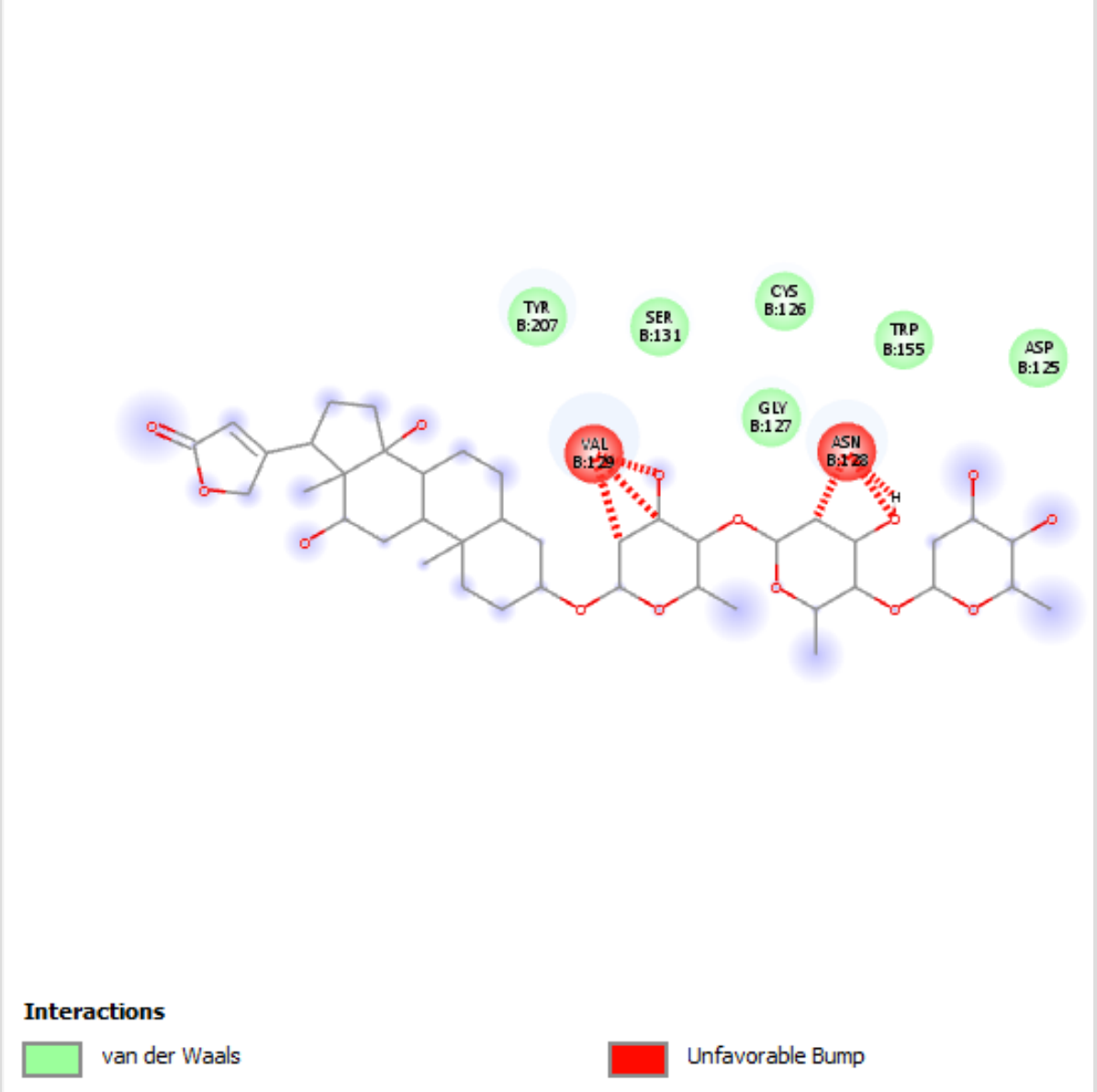
RESULTS

Conformer ID	Protein 7DDH	Binding Affinity(kcal/mol)	Inhibition Constant × 10 ⁻⁶
46173848	Bufadienolide	-8.6	0.496
2724385	Digoxin	-10.0	0.0467

Figure 5. Bufadienolide



Figures 6. Digoxin



DISCUSSION

The binding affinity of bufadienolide is -8.6 kcal/mol and high compared to digoxin which -10kcal/mol for the Na/K ATPase pump (Protein 7DDH). But it is observed digoxin has unfavourable interactions with VAL 129 and ASN 128 proteins which maybe an indication for toxicity and unfavourable protein-ligand interaction. Bufadienolide interaction shows van-der waals, alkyl and pi-alkyl interaction with the Na/K ATPase pump. Thus, bufadienolide present in *Bryophyllum pinnatum* is an emerging cardiac glycoside

CONCLUSIONS

Like Digoxin, bufadienolide has strong binding affinity for the NA/K ATPase and have ability to perform the same therapeutic effect and with no unfavorable interaction with the protein. These findings highlight the potential of bufadienolides as alternative treatments for heart failure.

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